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# THE JOHNS HOPKINS HOSPITAL REPORTS

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# JOHNS HOPKINS HOSPITAL

# REPORTS

VOLUME XV

BALTIMORE
THE JOHNS HOPKINS PRESS
1910

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The Lord Baltimore Press
BALTIMORE, MD., U. S. A.

# CONTENTS


I. A Bacteriological and Clinical Study of a Series of Seventy-four Cases of Diarrhœa in Children. By J. H. Mason Knox, Jr., M. D., and Edwin H. Schorer, M. D. ..... 1

II. An Analytical Study of Acute Lobar Pneumonia in the Johns Hopkins Hospital, from May 15, 1889, to May 15, 1905. By J. A. Chatard, M. D. ..... 55

III. A Pathological Analysis of 195 Cases of Lobar Pneumonia. By Marshal Fabyan, M. D. ..... 81

IV. The Leucocytes in Acute Lobar Pneumonia. By J. A. Chatard, M. D. ..... 89

V. An Analytical Study of Terminal Pneumonia. By J. A. Chatard, M. D. ..... 99

VI. The Termination of Pneumonia in Cases with Recovery. By Charles P. Emerson, M. D. ..... 103

VII. Acute Endocarditis with Lobar Pneumonia. By Harry T. Marshall, M. D. ..... 139

VIII. Acute Pericarditis Complicating Acute Lobar Pneumonia. By J. A. Chatard, M. D. ..... 155

IX. Empyema in Acute Lobar Pneumonia. By Thomas McCrae, M. D., F. R. C. P. ..... 167

X. Peripheral Venous Thrombosis in Pneumonia with Report of Three Cases and a Review of Those Previously Recorded. By Walter R. Steiner, A. M., M. D. ..... 189

XI. Pneumococcic Arthritis. By Campbell P. Howard, M. D. ..... 229

XII. Pneumococcus Meningitis. By Frederic M. Hanes, M. D. ..... 247

XIII. Delayed Resolution in Lobar Pneumonia. By Thomas McCrae, M. D., F. R. C. P. ..... 277

XIV. Skin Transplantation. With a Review of 550 Cases at the Johns Hopkins Hospital. By John Staige Davis, M. D. ..... 307

XV. Epidemic Cerebrospinal Meningitis and Serum Therapy at the Johns Hopkins Hospital. By Frank J. Sladen, M. D. ..... 397

# ILLUSTRATIONS


1. Chart showing the yearly number of patients with pneumonia and their mortality (Chart 1) ..... 56
2. Do. (Chart 2) ..... 58
3. Do. (Chart 3) ..... 61
4. Do. (Chart 4) ..... 72
5. Chart showing number of cases of pneumonia and mortality percentage of same (Chart 1) ..... 92
6. Do. (Chart 2) ..... 97
7. Simple crisis. The large figures below are the leucocyte counts (Chart 1) ..... 106
8. Crisis in the case of an infant, showing the deep drop and high leucocyte counts (Chart 2) ..... 107
9. Pseudocrisis on seventh day (Chart 3) ..... 118
10. Protracted crisis (Chart 4) ..... 119
11. Protracted crisis. Critical fall of blood-pressure (Chart 5) ..... 123
12. Lysis (Chart 6) ..... 126
13. Crisis with collapse (Chart 7) ..... 136
14. Peripheral venous thrombosis in pneumonia. Case I (Chart 1) .192, 193
15. Do. Case I (Chart 2) ..... 197
16. Do. Case II (Chart 3) ..... 200, 201
17. Admission on the eighth day of the pneumonia (Fig. 1) ..... 287
18. Admission on the second day of the attack of pneumonia (Fig. 2) . 288
19. Admission on the fourth day of the attack of pneumonia (Fig. 3) .. 293
20. Admission on the fifth day of the pneumonia (Fig. 4) ..... 294
21. Smith's scissor forceps for cutting Reverdin grafts (Fig. 1) ..... 313
22. The boards in place holding the skin of the thigh flat and taut (Fig. 2) ..... 315
23. The cutting is nearly completed. The graft is held up by an instrument (Fig. 3) ..... 316
24. Shows the area from which this small graft was cut (Fig. 4) .... 317
25. Complete take, Thiersch graft, on a breast wound at the first dressing, 10 days after grafting (Fig. 5) ..... 318
26. Complete take, Thiersch graft, about 2½ weeks after operation (Fig. 6) ..... 319
27. Healed graft which is firmly adherent to its bed (Fig. 7) ..... 320
28. Kortuem's knife for cutting Thiersch grafts (Fig. 8) ..... 323
29. Rehn's knife for cutting Thiersch grafts (Fig. 9) ..... 323
30. Thiersch's knife for cutting thin grafts (Fig. 10) ..... 323
31. Heavy razor for cutting Thiersch grafts (Fig. 11) ..... 323

32. Hoffman's guarded knife for cutting Thiersch grafts (Fig. 12) ..... 324
33. The Catlin amputating knife, which is used at the Johns Hopkins Hospital for cutting Thiersch grafts (Fig. 13) ..... 325
34. Scar on outer side of thigh due to cutting of Thiersch grafts (Fig. 14) ..... 327
35. Actual size of the openings of the rubber impregnated mesh used for splinting grafts (Fig. 15) ..... 328
36. Stump covered with whole-thickness grafts, which are held in place by the rubber impregnated meshed material, secured by adhesive straps (Fig. 16) ..... 329
37. Rubber impregnated meshed material over a graft placed on the granulating wound shown in Fig. 32 (Fig. 17) ..... 330
38. The rubber impregnated material splinting several whole-thickness grafts on an extensive ulcer of the back (Fig. 18) ..... 331
39. A whole-thickness graft splinted by the rubber impregnated material (Fig. 19) ..... 332
40. Cage over chest allowing exposure to the air of grafted area (Fig. 20) ..... 333
41. Front view of same cage, showing construction by the use of two ordinary wire splints (Fig. 21) ..... 334
42. Wire cage for the exposure of a stump of the foot to the air, after grafting (Fig. 22) ..... 335
43. The same cage looking from above downward (Fig. 23) ..... 336
44. Two pieces of superficial epidermis, obtained by Lusk's method, which were spread out on a glass slide and sterilized (Fig. 24). 337
45. The outline of a whole-thickness graft on the skin of the leg (Fig. 25) ..... 339
46. The same area, with the skin and subcutaneous fat cut through, down to the deep fascia, leaving the flap intact on its bed (Fig. 26) ..... 340
47. Method of trimming off the subcutaneous fat from a whole-thickness graft (Fig. 27) ..... 341
48. Small wire cages, front and lateral views (Fig. 28) ..... 343
49. Wire mesh cage on thigh, secured in place by adhesive straps (Fig. 29) ..... 344
50. Same cage from below (Fig. 30) ..... 345
51. The result of whole-thickness grafting on the palm of a contracted hand (Fig. 31) ..... 347
52. Large ulcer on the outer side of the thigh, which is covered with flat, healthy granulations (Fig. 32) ..... 348
53. Whole-thickness graft from a negro, which has taken on the abdominal skin of a dog (Fig. 33) ..... 350
54. Microphotograph of section through the graft, shown in Fig. 33 (Fig. 34) ..... 351
55. Section of the area from which a Thiersch graft was cut (Fig. 35) ..... 352

56. Section of the grafted skin with the stratum corneum partly detached (Fig. 36) ..... 353
57. The skin edge thrown into folds by the pursestring suture with the graft jointing it (Fig. 37) ..... 354
58. Stump of the upper third of leg, which was grafted completely 14 years ago (Fig. 38) ..... 356
59. Returning pigmentation in lines and patches in ulcers healed by the use of scarlet red ointment (Fig. 39) ..... 357
60. An ulcer of the outer aspect of leg (Fig. 40) ..... 360
61. Ulcer following burn of leg. The leg is in a plaster of Paris cage (Fig. 41) ..... 361
62. Israelson's double knife for the transplantation of mucous membranes (Fig. 42) ..... 362
63. Instruments used in making the lumbar punctures and injecting the serum (Fig. 1) ..... 406
64. A composite chart of the temperature, pulse, and respirations of the 23 cases on admission before the administration of serum.. 432
65. Epidemic cerebrospinal meningitis and serum therapy (Chart 1).. 479
66. Do. (Chart 2) ..... 482
67. Do. (Chart 3) ..... 485
68. Do. (Chart 4) ..... 488
69. Do. (Chart 5) ..... 491
70. Do. (Chart 6) ..... 493
71. Do. (Chart 7) ..... 496
72. Do. (Chart 8) ..... 498
73. Do. (Chart 9) ..... 501
74. Do. (Chart 10) ..... 503
75. Do. (Chart 11) ..... 505
76. Do. (Chart 12) ..... 507
77. Do. (Chart 13) ..... 512
78. Do. (Chart 14) ..... 514
79. Do. (Chart 15) ..... 516
80. Do. (Chart 16) ..... 519
81. Do. (Chart 17) ..... 522
82. Do. (Chart 18) ..... 523
83. Do. (Chart 19) ..... 525
84. Do. (Chart 20) ..... 527
85. Do. (Chart 21) ..... 534
86. Do. (Chart 22) ..... 536
87. Do. (Chart 23) ..... 538

# A BACTERIOLOGICAL AND CLINICAL STUDY OF A SERIES OF SEVENTY-FOUR CASES OF DIARRHŒA IN CHILDREN.*

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## Introductory.

Since the association of the dysentery bacillus with many instances of diarrhœa in infants and young children, it has been the endeavor of clinicians by careful analysis of their cases, to determine whether infection with this organism produced in these young patients any symptoms, or group of symptoms, which would serve to distinguish these cases from the diarrhœa of other causes.

Such clinical analysis was attempted by one of us in two series of cases occurring during the summers of 1902 and 1903, respectively at The Thomas Wilson Sanitarium,[1] and in a smaller number of similar cases by Strong[2] and by Pease & Shaw[3] and others.

The investigation of the clinical side of the problem formed an important part of the extensive studies carried on during the summer of 1903 by many workers in several of the large cities in the country, under the direction of The Rockefeller Institute for Medical Research.[4] The results of these studies included an examination of 237 cases, and indicated that the dysentery organism, or a member of the so-called dysentery group, could be found in the stools, or at autopsy in the intestines of many instances of diarrhœa in young children, that the proportion of cases in which this organism was found depended largely upon the skill and experience of the investigator, and moreover, that nearly every clinical variety of the diarrhœas occurring

* The cases occurred at The Thomas Wilson Sanitarium during the summer of 1904, and the studies were carried on with the aid of a grant from The Rockefeller Institute for Medical Research.

in summer, except cholera infantum, was included in the number associated with the dysentery organism, and that it seemed impossible to separate by any special symptoms or signs the infected from the non-infected cases. The differences that have been shown by Kruse, Martini and Lentz, Flexner, Hiss and Russell, Park and others, to exist in the various isolations of the dysentery bacilli have been of interest to the pediatrician inasmuch as it has been shown that the dysentery organisms obtained from infants suffering with diarrhœa belonged for the most part to the Flexner-Harris type and differed slightly from the variety of the organism first described by Shiga.

In the studies here reported a systematic effort was made to determine in every case not only the types of the infecting dysentery bacillus, but also the presence or absence of other pathogenic organisms, notably the streptococcus pyogenes and of all organisms which agglutinated with the blood serum of the patient. By this method it was hoped to study all the bacteria which could be casually associated with the intestinal disorders and to determine their relation, if any, to the dysentery bacillus. The cases presented, seventy-four in number, represent seriatim the infants suffering from diarrhœa, admitted to the wards of The Thomas Wilson Sanitarium, during the months of June, July and August, 1904. They have been divided into groups as far as possible according to the types of the pathogenic organism found in the stools or at autopsy. A number of cases were studied in each of which more than one variety of the dysentery bacilli was found. These are considered together, but are so arranged that the exact combination of types is specified in each instance. It was thought that in this way the relative frequency of the several strains of dysentery bacilli and of the pathogenic organisms in the intestinal tract of infants suffering from diarrhœa, could be more clearly indicated, and the relation of the clinical features of the illness to the particular types of the infective agent easily studied.

The majority of our cases were of severe grade. Many of them were not brought to the Sanitarium until their condition was grave. They have been divided clinically into these groups:

A. Inflammatory cases, ileo-colitis, 29 in number or 39%.

B. Toxic cases, dyspeptic or fermental diarrhœa, 36 in number or 48%.

C. Intestinal indigestion, 7 in number or 11%.

D. Chronic gastro-enteritis, one case.

E. Tuberculous ileo-colitis, one case.

In 20 of the cases mal-nutrition was a marked feature. It was thought unwise to attempt to further subdivide our cases. It is doubtful if our series included any of the nervous diarrhœas in the classification recently suggested by Dunn.[3] When the anatomical diagnosis at autopsy differed from the clinical the former was adopted. So much confusion exists as to terminology that one interested can best determine the nature of the illness in any case by consulting the abstract of the history.

The result of treatment for the whole series was as follows:

| | |
|---|---|
| Recovered completely | 30 or 40.5% |
| Improved | 1 or 16 |
| Unimproved | 1 or 1.5 |
| Died | 31 or 42 |

Laboratory studies of the organisms isolated were carried on both during the summer and through the following winter. Great care was taken to determine accurately the type to which each isolation of dysentery bacilli belonged. The agglutination reaction of all these strains was thoroughly tested. The results of the laboratory work are first considered and later the clinical aspect of the cases associated with the various organisms and the types of dysentery bacilli is discussed.

We regarded as *B. dysenteriæ* all organisms having the following characteristics, viz.: short oval, non-motile bacilli, decolorizing by Gram's method, producing round, moist pale colonies on agar, not liquifying gelatine, showing on potato an almost invisible dry white growth becoming reddish-brown with age, producing in milk an initial acidity and after 5-10 days again restoring the original color to the medium, producing a cloudiness with some sediment in bouillon but no pellicle, not producing gas in any sugar medium but producing a definite acidity with certain fermentable substances.

We preferred investigating naturally passed stools to methods by which the contents of the bowel are obtained by the introduction of tubes, because with tubes the material from the lumen is obtained rather than from the intestinal wall. In a naturally passed stool, especially when this is partly fecal, one finds mucus or mucus and pus on the sides of the fecal material and thus can select the material

coming from a point nearest the intestinal lesion. It is possible that the method of collecting the stool and selecting the portion of it to be examined may account for the failure to find *B. dysenteriæ* in many of the cases elsewhere reported.

After making our isolations dysentery-like organisms were tested with the patient's blood in dilutions of 1 : 20 and 1 : 50 and with Mulford's anti-dysenteric serum in dilutions of 1 : 50 and 1 : 100. All other organisms were also tested for agglutination with the patient's blood. Organisms other than *B. dysenteriæ* agglutinating with the patient's blood and all streptococci were tested for pathogenicity by intra-peritoneal inoculation into guinea-pigs.

Whenever *B. dysenteriæ* was not found in the first specimen of stool, subsequent stools from the same case were examined until dysentery bacilli were found, the case had recovered, or the patient had died. If the organism was not found during life cultures were taken from scrapings of the large intestines after death, and when an autopsy could be obtained cultures were also made from the heart's blood, spleen, and mesenteric glands.

### Summary of Bacteriological Findings.

The material used for examination showed microscopic or macroscopic blood in 30 cases, mucus in 66 and pus in 31 cases. In 53 of the cases, or 71.6%, dysentery bacilli were found. From 11 cases with mucus and blood *B. dysenteriæ* was found 25 times in 7 cases; from 15 cases with mucus, blood and pus, 68 isolations were made from 14 cases; from 12 cases with mucus and pus 47 cultures were obtained from 11 cases; and from 26 cases where mucus only was present, 32 isolations were made from 14 cases. From this it is seen that *B. dysenteriæ* was found in 63.6% of the cases with mucus and blood with an average of 3.5 cultures per positive case; in 93.3% of the cases with mucus, blood and pus, with an average of 4.7 colonies per positive case; in 92.5% of the cases containing mucus and pus with an average of 4.27 isolations per positive case. Our experience would therefore indicate that the cases containing microscopic or macroscopic pus are the most favorable for the isolation of *B. dysenteriæ* as the bacillus was found in from 92.5% to 93% of such cases with an average of from 4.27 to 4.7 colonies per positive case.

In eight, or 10.8%, of the cases investigated the dysentery organ-

ism was found in the first specimen examined, in 10, or 13.5%, of the cases it was found in the second specimen of stool, in 7, or 9.4%, of the cases in the third specimen, and in 7, or 9.4%, of the cases four or more specimens were examined before finding *B. dysenteriæ*. In 17, or 22.8%, of the cases, the dysentery bacillus was not found until the large bowel had been scraped, and in two cases the bacillus was obtained from the scrapings, when no stool specimen had been obtained. In two cases the specific organism was found at autopsy outside of the intestinal tract, once in the liver, once in the mesenteric gland, and in one case an organism like *B. dysenteriæ* was found in the heart's blood. This organism is not agglutinated by anti-dysenteric serum.

In 11 of the 53 cases in which *B. dysenteriæ* was found streptococci were also obtained. Of the 21 cases not containing the bacillus of dysentery 6 contained streptococci. From two cases *B. coli communis* agglutinating with the patient's blood was found, and in two cases agglutinating pathogenic *B. pyocyaneus* was isolated.

In 10, or 13.5%, of the cases no dysentery bacilli, streptococci or agglutinating micro-organisms could be found, and in 21 or 28.4%, of the cases no dysentery organisms could be isolated.

The number of dysentery bacilli varies greatly. Some cases present an almost pure culture of *B. dysenteriæ*, while in others they can be isolated only with the greatest difficulty. This is illustrated by two cases in which at autopsy diphtheritic membranes were found. The last of our cases, Clinical No. 293, presented at autopsy a green membrane in the colon, from which suspensions and cultures were made and yielded an almost pure culture of *B. dysenteriæ*. In contrast to this, in another case, Clinical No. 76, which at autopsy had a marked membrane in the lower part of the small intestine and in the large intestine, no dysentery bacilli could be isolated from plates made from suspensions of the membrane.

## Fermentations.

The differences in the fermentation properties of the dysentery group of organisms have become of importance since Martini and Lentz [6] and Hiss and Russell [7] divided dysentery bacilli into sub-groups on the basis of fermentation of various carbohydrates and the alcohol mannite. MacConkey and Hill [8] had before this found that the dysen-

tery bacilli of which they were able to obtain cultures differed in the fermentation of mannite, but as they were making no special study of the dysentery group the difference was not referred to in the text of their article. In December, 1904, Hiss[6] presented a study of cultures of dysentery bacilli which he obtained from various sources. He divides the group of dysentery bacilli into two distinct sub-groups, those fermenting mannite and those not fermenting mannite. The mannite fermenters he again divides into three varieties, which he says are "separated into groups by differences which we have reason to believe are not, so far as fermentation goes, fundamental, but are nevertheless clearly marked."

In testing our isolations we have used dextrose, galactose, levulose, maltose, saccharose, lactose, dextrin, mannite and inulin. As a nutrient medium Hiss's serum-water was used as described by Hiss and Russell.[7] It is easily made and is sugar free.* Control tests were often made with Smith's fermentation tubes, and it was found that acid formation in serum-water agrees with acid formation in the open arm, and need not be the same as in the closed arm of the tube, so that in all of our experiments acid fermentation and coagulation agree with the results in the open arm of the fermentation tube.

Besides fermentation reactions, indol tests and cultures on milk were made. All of our fermentation tests were repeated at least three times, while the organisms selected to represent the different groups were re-tested many times.

As was pointed out by Hiss, it is necessary to extend fermentation tests over a number of days, inasmuch as certain fermentations occur much later than others. For this reason we have made two classifications, one for five days and one for twenty-five days. These classifications generally agree with the exception that in twenty-five days fermentation Groups III and II are the same, but that these groups are not identical is seen from the early fermentation and agglutination tests.

In our study were included 172 cultures of *B. dysenteriæ* isolated

* It consists of beef serum one part, distilled water two parts, aqueous solution of litmus sufficient to color. To this 10 grams of the fermentable substance to be tested is added for each litre of the medium. The medium is put into tubes and fermentation is tested for by the reddening and coagulation of the medium.

during the summer of 1904, 10 isolations obtained from Bassett, and 18 cultures from various other sources.

All of these cultures fell into the four groups described by Hiss, as follows in Table I:

TABLE I.

*5 Day Fermentation.*

| | I Shiga | II Hiss "Y" | III Strong | IV Flexner-Harris | "B" Duval & Schorer |
|---|---|---|---|---|---|
| Dextrose | Coag. | Coag. | Coag. | Coag. | Coag. |
| Levulose | Coag. | Coag. | Coag. | Coag. | Coag. |
| Galactose | Coag. | Coag. | Coag. | Coag. | Coag. |
| Mannite | Neg. | Coag. | Coag. | Coag. | Coag. |
| Lactose | Neg. | Neg. | Neg. | Neg. | Neg. |
| Saccharose | Neg. | Neg. | Acid | Coag. | Neg. |
| Maltose | Neg. | Neg. | Neg. | Coag. | Coag. |
| Dextrine | Neg. | Neg. | Neg. | Coag. | Coag. |
| Litmus Milk | Neg. | Neg. | Neg. | Neg. | Neg. |

*25 Day Fermentation.*

| | I Shiga | II Hiss "Y" | III Strong | IV Flexner-Harris | "B" Duval & Schorer |
|---|---|---|---|---|---|
| Dextrose | Coag. | Coag. | Coag. | Coag. | Coag. |
| Levulose | Coag. | Coag. | Coag. | Coag. | Coag. |
| Galactose | Coag. | Coag. | Coag. | Coag. | Coag. |
| Mannite | Neg. | Coag. | Coag. | Coag. | Coag. |
| Lactose | Neg. | Neg. | Neg. | Neg. | Acid |
| Saccharose | Neg. | Coag. | Coag. | Coag. | Acid |
| Maltose | Acid | Coag. | Coag. | Coag. | Coag. |
| Dextrine | Neg. | Neg. | Neg. | Coag. | Coag. |
| Litmus Milk | Neg. | Neg. | Coag. | Neg. | Acid |

*Group I.*—Ferments the monosaccharids only during the first five days, but later also ferments maltose; however, not producing a coagulum in the serum-water. This group is represented by the Shiga culture sent to this country.

*Group II.*—Ferments monosaccharids and mannite early while after twenty days saccharose and maltose serum-water are coagulated. This group is represented by the Hiss and Russell "Y" organism.

*Group III.*—Ferments early the monosaccharids, mannite, and saccharose, while maltose serum-water is coagulated after twenty-five days. This group is represented by the Strong culture.

*Group IV.*—Ferments the monosaccharids, mannite, maltose, dextrin and saccharose readily. This group is represented by the Flexner-Harris culture.

It is seen that although Groups II and III are alike in late fermentation, Group III forms acid in saccharose very early, while Group II forms it only late. There are also definite agglutination differences, as will be seen later.

The different groups were not found to be limited to particular cases, but often were found together in the same case. Our isolations of the summer of 1904 were divided among the four groups as follows:

Group I was found 34 times in 14 cases, being the only type found in 4 cases.

Group II organisms were found 91 times in 25 cases, in 14 of which it was the only type represented.

Group III type was found 3 times in one case, other types being found in the same case.

Group IV organisms were isolated 44 times from 16 cases and was the only type represented in 6 cases.

From this it is seen that Hiss and Russell's "Y" type represents by far the largest group, while the Flexner-Harris type of organism is the next most frequently found.

Of the 28 cultures of *B. dysenteriæ* isolated by various investigators, and which were studied at the same time as those obtained from our own cases, 4 belonged to Group I, 13 to Group II, and 2 to Group IV.

In addition to the dysentery organisms producing a typical reaction in litmus milk we isolated several bacilli which Torrey [10] has called "dysentery-like" or "pseudo-dysentery" organisms. These bacilli were described by Duval and Schorer,[11] later by Duval,[12] and Torrey [6] has recently reported a study of the entire group. They have been divided into several varieties, thus—

Bacillus "A" (Duval and Schorer) ferments the monosaccharids, mannite, and lactose and not dextrin or saccharose.

Bacillus "B" (Duval and Schorer) ferments after five days the monosaccharids, mannite, lactose, maltose and dextrin; while after ten to fifteen days it also ferments saccharose.

Bacillus "C," the bacillus described by Duval, after five days ferments the monosaccharids, mannite, lactose, saccharose, maltose and dextrin.

During the summer of 1904 we isolated 7 cultures corresponding to description of Bacillus "B," from 3 cases, in 2 cases of which no dysentery bacilli were found. All of these cultures fermented lactose

and saccharose after some time, and in every instance saccharose was fermented earlier by Duval's culture, Bacillus "C" than by our own isolations.

We obtained no isolations of the other groups of lactose fermenting organisms than those belonging to the group represented by Bacillus "B."

An interesting type of bacillus was isolated from two of our cases. This bacillus is slightly motile, does not stain by Gram's method; the colonies on agar resemble those of *B. dysenteriæ*. It does not liquify gelatine, and on milk ultimately produces some alkalinity. This bacillus produces in Hiss's semi-solid media a slightly branching growth, there being produced a firm growth in the line of inoculation. Its action on the carbo-hydrates is interesting, inasmuch as it ferments the monosaccharids, dextrose and levulose, while another monosaccharid galactose is not acted upon. In the fermentation tube there is growth in the open arm in dextrose, levulose and galactose, but in dextrose and levulose there is an acid formation, while in galactose there is none. So far as we know this organism has not been described before.

## Agglutinations.

Our studies of the agglutination properties of the organisms isolated may be considered under the following captions:

### *A. Serum Reaction for Identification of B. Dysenteriæ.*

From the earliest experience with the dysentery bacillus it has been shown that for the identification of the suspected organisms isolated from the dejecta of patients, agglutination tests with a specific immune serum are of great importance. For this purpose we used Mulford's anti-dysenteric horse serum in dilutions of 1-50 and 1-100. All bacilli which did not agglutinate with the specific serum were not regarded as dysentery bacilli, while those which did react promptly in the dilutions indicated were further studied and identified by their cultural and fermentative properties.

### *B. Agglutination with the Patients' Blood.*

(1) Of organisms belonging to the dysentery group.

The agglutinations with the patients' blood were tried on stock cultures of *B. dysenteriæ* (Flexner-Harris) and *B. dysenteriæ* isolated

from the same case. The dilutions were either 1-20 or 1-50 and made in hanging drop.

Of the 74 cases examined, blood was obtained from 54 patients. Of these bloods 47.7% agglutinated the Flexner-Harris organism, while 65.7% of the same bloods agglutinated the dysentery organism isolated from the case. Of 18 cases, the blood of which would not agglutinate the Flexner-Harris organism, 14 yielded isolations of *B. dysenteriæ*. The blood from 4 cases, in the stools from which *B. dysenteriæ* was not found agglutinated the Flexner-Harris organisms. The blood from 51.5% of the cases from which *B. dysenteriæ* was isolated agglutinated the Flexner-Harris type of the dysentery group, while the blood from 61.6% of the same series agglutinated the organism isolated.

The importance that is to be attached to agglutination of *B. dysenteriæ* with patient's blood has been much discussed and from the work of Martini and Lentz [8] it is evident that the patient's serum is not suitable for the identification of infection with *B. dysenteriæ*. The investigation of the development of agglutinins is of considerable importance. Winne [18] working at The Thomas Wilson Sanitarium in 1903 reports positive agglutination with the blood of the patient in dilutions of 1-100 in 26 instances, or 65% in a study of 40 cases in which *B. dysenteriæ* was found. Our percentage for the same class of cases was somewhat lower, namely, 51.5%. Our results indicate that the serum obtained from patients in which dysentery bacilli were found, agglutinates the organism isolated in 14.2% more instances than it agglutinates the stock culture of the Flexner-Harris type. This suggests that agglutinins are formed in response to the organisms found in the body of the patient. The fact, however, that 14 out of 18 cases not agglutinating the Flexner-Harris type of *B. dysenteriæ*, contain the dysentery bacillus and that four cases from which no dysentery bacilli could be isolated yet agglutinated the Flexner-Harris organism, makes it evident that agglutination tests with the blood of the patient cannot be relied upon to determine infection with *B. dysenteriæ*.

(2) Agglutination of micro-organisms other than *B. dysenteriæ* with the blood of the patient.

As was mentioned earlier in this paper we tried not only to isolate *B. dysenteriæ*, but also all streptococci and organisms that agglutinated

with the blood of the patient. We had expected to find a larger number of cases in which the blood of the patient would agglutinate organisms other than *B. dysenteriæ*, but out of the 54 cases from which we obtained blood only 5 agglutinated the other organisms isolated. From two of these cases *B. coli communis* was isolated. The bacilli in both cases agglutinated in dilutions of 1 : 50 with the patient's blood and were found to be pathogenic. From three other cases we isolated *B. pyocyaneus*, which bacilli agglutinated with the blood of the patient in dilution of 1 : 50. In one of these cases the organism was not pathogenic.

### *C. A Study of the Agglutinins for the Types of the Dysentery Group.*

Concerning the agglutinations with sera of high agglutinating value there is already a large literature. Agglutination tests have been used as a basis of classification of the different strains of *B. dysenteriæ* and also for their practical bearing in curative and prophylactic sera.

Hiss in his paper concluded that there were wide differences in the agglutination characters of the different groups of dysentery bacilli. When any one type of *B. dysenteriæ* is used to immunize an animal there develops in the body not only its own agglutinins but also agglutinins for some of the other types of dysentery bacilli. From this has developed a study of specific and accessory agglutinins upon which Hiss,[9] Eisenberg[14] and Torrey[10] have written extensively.

Eisenberg finds that absorption with the Shiga variety of dysentery bacilli, removes from an immune serum also a part of the agglutinins affecting the Flexner-Harris type, while on the other hand the Flexner-Harris bacillus absorbs its own and only a few other agglutinins. Shiga filtrate will absorb the precipitins for the Shiga group as well as those of the Flexner-Harris group, while the Flexner-Harris organism absorbs only its own precipitins. Moreover, inasmuch as Eisenberg finds that normal horse serum will agglutinate the Shiga strain in dilutions of only 1-10 or 1-20, while it will agglutinate the Flexner-Harris type in dilutions of 1-75 or 1-375, he thinks that this may be the reason for the greater ease of production of Flexner-Harris serum.

Hiss has found that absorption tests show that the major agglu-

tinins developing in the serum of animals inoculated with representatives of these groups are distinct and specific, but can be removed by saturation of the serum with the homologous organism or one of its group or species.

In our experiments on absorption we used cultures selected to represent each of the groups as determined upon by fermentation tests. The sera we used were obtained from various sources.

I. Immune curative serum kindly sent us from Japan by Dr. Shiga.

II. Flexner-Harris goat serum sent us by Dr. Flexner.

III. Hiss's "Y" serum sent us by Dr. Hiss.

IV. Serum from a rabbit immunized by us to the Shiga group of organisms.

V. Serum from a rabbit immunized by us to the Strong group (Group III) of dysentery bacilli.

With these five immune sera we determined the maximum dilution at which agglutination would occur with the various groups of dysentery bacilli. Next we absorbed each serum with each of the groups and tested the limit of dilution at which the remaining groups would agglutinate, and lastly we absorbed each serum with all of the combinations of four types and tested the limit of agglutination of the fifth type. In this way we have approached as nearly as is possible with the now known groups, to specific agglutinins.

The agglutinations were made in small tubes. Cultures were made on slant agar, the growth being suspended in salt solution of which one cubic centimeter was used for each agglutination test. All dilutions of serum and cultures were made with salt solution. The absorptions and agglutinations were incubated at 37° C. for about twenty hours when readings were made with a small hand lens.

In absorption tests the amount of culture necessary to completely absorb a given type was first determined and when absorbing with four groups a total amount of the culture required to completely absorb the agglutinins when tested singly, was added. No absorption was considered complete unless tested for in the agglutination tube. After absorption the serum was centrifugalized until clear. The lowest dilutions tested were 1-100.

The results of our experiments are as follows:

TABLE II.

*Shiga Curative Serum.*

| After absorption with | Agglutination. | | | | |
|---|---|---|---|---|---|
| | I. | II. | III. | IV. | "B" |
| | —100 | 500 | —100 | 800 | 5000 |
| I. | 0 | 500 | —100 | 800 | 5000 |
| II. | —100 | 0 | —100 | —100 | 3000 |
| III. | —100 | 500 | 0 | 800 | 5000 |
| IV. | —100 | 100 | —100 | 0 | 1000 |
| "B" | —100 | 200 | —100 | 100 | 0 |
| II, III, IV, "B" | —100 | | | | |
| I, III, IV, "B" | | —100 | | | |
| I, II, IV, "B" | | | —100 | | |
| I, II, III, "B" | | | | —100 | |
| I, II, III, IV. | | | | | 2500 |

Table II shows the agglutination results obtained with the curative serum sent by Shiga. It is evident that the serum agglutinates Group "B" in the highest dilutions, but also Groups II and IV in lower dilution, and that the serum does not agglutinate either Groups I or III. It is likewise seen that absorption with Group "B" takes agglutinins for both Groups II and IV; Group II reduces the agglutinating value for Groups IV and "B"; and Group IV reduces the agglutinins for Groups II and "B." Thus absorption with any of the Groups II, IV or "B" reduces the agglutinating value for either of the other two groups. Absorption with all of the groups but "B" leaves a serum of high agglutinating value for "B."

TABLE III.

*Flexner-Harris' Goat Serum.*

| After absorption with | Agglutination. | | | | |
|---|---|---|---|---|---|
| | I. | II. | III. | IV. | "B" |
| | 100 | 1200 | 100 | 6000 | 1200 |
| I. | 0 | 1000 | —100 | 6000 | 1200 |
| II. | —100 | 0 | —100 | 3000 | 800 |
| III. | —100 | 500 | 0 | 6000 | 500 |
| IV. | —100 | 300 | —100 | 0 | 500 |
| "B" | —100 | 1000 | 100 | 6000 | 0 |
| II, III, IV, "B" | —100 | | | | |
| I, III, IV, "B" | | —100 | | | |
| I, II, IV, "B" | | | —100 | | |
| I, II, III, "B" | | | | —1000 | |
| I, II, III, IV. | | | | | —100 |

The Flexner-Harris serum agglutinates the Flexner-Harris organism (Group IV) in dilutions greater than 1 : 6000, Group II in dilutions 1 : 1200 and Group "B" 1 : 1200. It is observed here that absorption with the Flexner-Harris organism reduces the agglutinating value of the serum for Groups II and "B" about equally and that absorption with Group II reduces the agglutinins for Group "B," while absorption with Group "B" reduces those for Group II but little. Absorption with Groups I, II, III and "B" does not take all of the agglutinins for Group IV.

TABLE IV.

*Hiss "Y" Serum.*

| After absorption with | Agglutination. | | | | |
|---|---|---|---|---|---|
| | I. | II. | III. | IV. | "B" |
| | —100 | 2500 | 300 | 1400 | —100 |
| I. | 0 | 2500 | 300 | 1400 | —100 |
| II. | —100 | 0 | —100 | 500 | —100 |
| III. | —100 | 2500 | 0 | 100 | —100 |
| IV. | —100 | 2500 | 100 | 0 | —100 |
| "B" | —100 | 2500 | 100 | 800 | 0 |
| II, III, IV, "B" | 0 | | | | |
| I, III, IV, "B" | | 2500 | | | |
| I, II, IV, "B" | | | —100 | | |
| I, II, III, "B" | | | | —100 | |
| I, II, III, IV. | | | | | —100 |

Serum of a rabbit immunized to Hiss "Y" culture or Group II produces no agglutinins for Groups I and "B," but does produce them for Groups II, III and IV. Absorption with Group II takes the agglutinins for Group III and some of those for Group IV; absorption with Group III reduces the number of agglutinins for Group IV, and absorption with Group IV takes up some of those of Group III. Absorption with Groups I, III, IV and "B," however, did not reduce the agglutinating value of the serum for Group II. It is to be noticed that Group II absorbs some of Group III agglutinins, but that Group III does not take up those of Group II.

TABLE V.

*"Shiga" Type Serum.*

| After absorption with | Agglutination. | | | | |
|---|---|---|---|---|---|
| | I. | II. | III. | IV. | "B" |
| | 1000 | —100 | 50 | 25 | —100 |
| I. | 0 | —100 | —100 | —100 | —100 |
| II. | 1000 | 0 | —100 | —100 | —100 |
| III. | 500 | —100 | 0 | —100 | —100 |
| IV. | 1000 | —100 | —100 | 0 | —100 |
| "B" | 1000 | —100 | —100 | —100 | 0 |
| II, III, IV, "B" | 400 | | | | |
| I, III, IV, "B" | | —100 | | | |
| I, II, IV, "B" | | | —100 | | |
| I, II, III, "B" | | | | —100 | |
| I, II, III, IV. | | | | | —100 |

A rabbit immunized with a Shiga culture produces an almost specific serum as Groups II and "B" are not agglutinated by the serum, and Groups III and IV only agglutinate in dilutions of 1 : 50 and 1 : 25 respectively. The agglutinating value of the serum is not affected by absorption with any of the groups but Group III.

TABLE VI.

*"Strong" Type Serum.*

| After absorption with | Agglutination. | | | | |
|---|---|---|---|---|---|
| | I. | II. | III. | IV. | "B" |
| | 0 | 200 | 5000 | 500 | 0 |
| I. | 0 | 100 | 5000 | 500 | —100 |
| II. | —100 | 0 | 5000 | 200 | —100 |
| III. | —100 | —100 | 0 | 100 | —100 |
| IV. | —100 | 200 | 5000 | 0 | —100 |
| "B" | —100 | 200 | 5000 | 500 | 0 |
| II, III, IV, "B" | —100 | | | | |
| I, III, IV, "B" | | —100 | | | |
| I, II, IV, "B" | | | 4000 | | |
| I, II, III, "B" | | | | 100 | |
| I, II, III, IV. | | | | | 100 |

Serum from a rabbit immunized to the bacillus belonging to the Strong group, or Group III, contains agglutinins for Groups II, III and IV, the agglutination with Group III being positive in dilutions of 1 : 5000. It is thus seen that the agglutination value of the serum

is reduced to three groups, still absorption with all but Group III reduces the agglutinins for Group III but slightly. It is also noticed that absorption with Group II reduces the agglutinins for Group IV, while absorption with Group IV does not reduce the agglutinating value for Group II. Absorption with Group III greatly reduces the value of agglutination of the serum for Groups II and IV.

From the tables some general conclusions, which will hold in the majority of cases, may be drawn.

*Group I* absorbs but few agglutinins of the other groups, those of Group II being partially taken up in Group III immune serum. Group I agglutinins are partially taken up by Group III.

Absorption with *Group II* reduces the agglutinating value of all sera tested for Groups IV and "B," while the agglutinins of Group II are partially absorbed in some sera by Groups I, III, IV and "B." Group II agglutinins are not absorbed by other groups in Group II serum.

Absorption with *Group III* reduces the agglutinating value of some of the sera for Groups I, IV and "B." The agglutinins of Group III are absorbed by organisms belonging to Groups II, IV and "B" in some of the sera.

*Group IV* absorbs partially, in some sera, the agglutinins of Groups II, III and "B." The agglutinins of Group IV are in every case absorbed by Group II and from some sera by Groups III and "B."

*Group "B"* absorbs the agglutinins of Groups II, III and IV, while the agglutinins of Group "B" are absorbed by Groups II, III and IV.

The absorption of agglutinins by the various groups of *B. dysenteriæ* varies much with the variety of organism used in immunizing the animal. This is well seen in the tables for Groups II, IV and "B" immune sera, under absorption with Group III. In Shiga curative serum (Group "B") the agglutinins for Groups II, IV, and "B" are not absorbed by Group III, in Flexner-Harris serum (Group IV) those for Groups II and "B" are partly absorbed by Group II, and in Hiss's "Y" serum (Group II) the agglutinins for Group IV are partly absorbed by saturation with Group III organisms. Further study as suggested by Eisenberg's and Hiss's results may show that the production of specific and accessory agglutinins may vary with the animal used in immunization.

From our data on specific and accessory agglutinins it is evident that the Flexner-Harris serum has the largest amount of common agglutinins, agglutinating all five types studied by us. Moreover, the Flexner-Harris type of *B. dysenteriæ* is not as pathogenic when grown on artificial media as the members of the other groups. These facts would indicate that this variety of the dysentery bacillus is best adapted and most effective for active and for passive immunization.

## Clinical Data.

The whole series of cases, 74 in number, have been arranged in the following subdivisions according to the nature or type of the associated pathogenic organisms:*

A. Cases in which the alkaline (original Shiga) type of dysentery bacillus was alone found.

B. Cases in which the only variety of the dysentery organism found corresponded to Hiss's bacillus "Y."

C. Cases in which the Flexner-Harris was the only type isolated.

D. Combined cases, where several members of the dysentery group were present together.

E. Cases in which the variety of the dysentery bacilli present was not determined.

F. Cases in which an organism identical to Bacillus "B" of the "dysentery-like" group was the only pathogenic form isolated.

G. Cases in which pathogenic streptococci were present in addition to some members of the dysentery group.

H. Cases where streptococci were the only pathogenic organisms found.

I. Cases in which organisms other than dysentery bacilli and streptococci were found, and which were pathogenic and agglutinated with the patients' blood.

J. Cases with negative bacteriological findings.

* Jehle [15] has recently reported a series of cases infected with the Shiga and Flexner types of dysentery organisms, respectively. In the latter group he includes apparently all the varieties which ferment mannite with acid production corresponding to our Groups B, C, and D. He thinks the infection associated with the Shiga type of B *dysenteriæ* more virulent but less easily communicable than that produced by the Flexner strain. Our cases give no support to these conclusions.

*A. Cases associated with the Alkaline (The Original Shiga) Type of dysenteriæ.*

Abstracts of histories are as follows:

J. T. Age, four months. Clinical No. 137. Admitted July 14, 1904. No previous illness, but never robust. Fed on Horlick's Malted Milk. Present illness began three weeks before admission with vomiting and diarrhœa. Stools, mucoid, twelve to fifteen in twenty-four hours. No history of blood. On admission child was pale, fairly well nourished, with a rickety rosary. After admission there was progressive, gradual loss of weight. Stools, for most part, fæcal: three to eight in twenty-four hours. No elevation of temperature. Discharged August 28, unimproved.

*Diagnosis.*—Mal-nutrition, diarrhœa, (super-imposed).

M. S. Age, two months. Clinical No. 215. Admitted July 30, 1904. Child never ill before. Bottle-fed, largely on condensed milk. Illness commenced with green, mucous stools; occasionally streaked with blood. There had been fever and moderate restlessness. Child on admission was well nourished. No signs of rickets. General condition improved rapidly under treatment and the child was discharged well on August 13.

*Diagnosis.*—Dyspeptic diarrhœa.

H. R. Age, four months. Clinical No. 72. Admitted July 2, 1904. History of infected navel at two months. Diet consisted largely of condensed milk. Six days before admission stools became frequent, green and mucoid; never blood-tinged. No fever, but frequent vomiting. Thrush present in the mouth. Child admitted in collapse. Emaciated, listless, with fever; slightly cyanosed. Some bronchitis. No response to treatment, and child died July 5.

*Autopsy.*—A few areas of bronchial pneumonia in the lungs. The stomach and small intestines, for the most part, were pale except for occasional scattered areas of hemorrhage. Peyer's patches were swollen. Mucous membrane of the large intestine was congested.

*Diagnosis.*—Mal-nutrition; dyspeptic diarrhœa, terminal.

C. W. Age, eight months. Clinical No. 206. Admitted July 28, 1904. Never well. Fed on condensed milk. One week before admission bowels became loose; stools contained mucus and were occasionally blood-tinged. On admission child was very sparely nourished, rachitic. Systolic murmur at apex of heart. Moderate œdema of extremities. Child's condition remained unchanged for several days except for a progressive loss of weight. There was moderate pyurea. Stools improved in character and for the last ten days of the child's stay in the Sanitarium were practically normal. Child discharged August 27, well.

*Diagnosis.*—Mal-nutrition; ileo-colitis.

### Discussion.

*Clinical Diagnosis.*—Of these four cases infected by the Shiga type of the dysentery organism, *three* were primarily instances of malnutrition to which the intestinal derangement was added. These three were more or less emaciated on admission. In but one was there much elevation of temperature noted.

*Stools.*—In all, the onset of the bowel involvement had set in with diarrhœa and mucous stools. The character of the movements in one case (No. 206),[1] the presence of pus and blood seemed to indicate a definite inflammation of the intestinal wall and the diagnosis of ileo-colitis.

Nausea and vomiting were present in but two cases. Thrush was noted once.

*Age.*—The patients were all young, varying from two to eight months. They were admitted in July. Two of the infants were discharged "well," one "unimproved," and one died. The autopsy findings in the fatal case were negative, except for a few areas of intestinal congestion and the swelling of the lymphoid structures.

All four cases had been fed on condensed milk or proprietary foods.

### *B. Cases with Hiss's "Y" Type.*

The largest number of cases associated with a single variety of pathogenic organisms were those in whose stools were found only dysentery bacilli belonging to the type described by Hiss and Russell, Hiss "Y," or Group II, above described. These were fourteen in number. Abstracts of their histories are as follows:

**L. J. Clinical No. 2. Age, eight months. Weight, 9¾ lbs. Admitted June 6, 1904. Markedly emaciated. Rickety rosary. Diet condensed milk. Scaffold abdomen and dry, harsh skin. Child has been acutely ill for two weeks. Fever, frequent stools, vomiting. After admission the child had an irregular temperature, 99-104° F. Stools muco-purulent in character, six to ten in twenty-four hours, often streaked with blood. Died June 15.**

No autopsy.

*Diagnosis.*—Ileo-colitis.

**J. H. Clinical No. 18. Age, five weeks. Weight 6½ lbs. Admitted June 18, 1904. Fed after the fourteenth day on condensed milk. Four days before admission acute symptoms began with numerous green,**

mucous stools, excessive vomiting and moderate fever. Nervous symptoms marked, and child admitted in semi-comatose condition with appearance of intestinal intoxication. Child remained in this condition until its death, four days later.

*Autopsy.*—Intestines found pale and thin throughout, except for occasional small hemorrhagic areas. Liver slightly fatty. Moderate œdema of base of brain was present.

*Diagnosis.*—Mal-nutrition, dyspeptic diarrhœa, severe.

W. W. Clinical No. 28. Age, two and one-half months. Admitted June 24, 1904. No disease before present illness. Fed on condensed milk. One week before admission stools became loose, numerous and mucoid in character. There was moderate vomiting. Child's general condition was never alarming. It was fairly well nourished. Stools became normal under treatment. The child was discharged well in two weeks.

*Diagnosis.*—Dyspeptic diarrhœa.

S. C. Age, six months. Clinical No. 6. Patient was a sparely-nourished colored child. Previous feeding had been broth, whole milk, and proprietary foods. No history of definite, acute illness was obtained. Stools, for most part, homogeneous, formed, occasionally, with curds, and mucus. Child vomited frequently, but on the whole, did well, and was discharged within six weeks, improved.

*Diagnosis.*—Gastro-intestinal indigestion.

F. E. Age, eight months. Clinical No. 128. Admitted July 12, 1904. The acute illness began three weeks before, with diarrhœa and vomiting. Stools were not more than six in twenty-four hours: contained mucus. Blood was noted once only. Little or no fever. Marked loss of weight. Child was well nourished on admission. Physical examination, negative. Under treatment the child rapidly improved. Stools became fæcal. Child was discharged July 19, well.

*Diagnosis.*—Dyspeptic diarrhœa.

A. S. Clinical No. 166. Age, seven months. Admitted July 20, 1904. Had been previously fed on condensed milk. Ten days before admission child was suddenly taken ill with vomiting and diarrhœa. Stools, eight to twelve in twenty-four hours, consisted largely of mucus, occasionally blood-stained. Child was admitted almost in collapse. Sunken eyes, rapid pulse, depressed fontanelles. Temperature varied from 90°-103°. Child's condition markedly improved, stools became fæcal after several days. Discharged August 3, well.

*Diagnosis.*—Dyspeptic diarrhœa; severe.

M. S. Clinical No. 171. Age, four months. Admitted July 21. Previous feeding condensed milk. Three and a half weeks before admission child had suffered an acute attack of diarrhœa from which he had never

completely recovered. Was restless and fretful and in frequent pain. Weighed on admission eight pounds. There was pronounced rosary and epiphyseal swellings. Abdomen distended. Case improved under treatment. There were usually three to five stools a day, often slightly lumpy. No blood was noticed. Child discharged August 23, improved.

*Diagnosis.*—Gastro-enteritis, chronic.

E. S. Clinical No. 175. Age, one month. Admitted July 21, 1904. Previous feeding, condensed milk. Weight five pounds. Had a purulent bilateral ophthalmia, thrush, and the stigmata of rickets. Two days before admission vomiting and diarrhœa had set in. Stools soon became mucous in character, eight to ten in twenty-four hours. No blood was noticed. Child did not respond to treatment. Temperature often subnormal. Died July 26.

*Autopsy.*—The whole gastro-intestinal tract was found to be hyperæmic. Solitary follicles everywhere enlarged. Occasional deep punched-out ulcers occupied the center of the follicles near the ileo-cæcal valve. Mucosa of large intestine for most part was intact. Marked enlargement of mesenteric lymphatic glands.

*Diagnosis.*—Ileo-colitis, acute.

B. M. Clinical No. 198. Age, five months. Admitted July 8, 1904. No previous illness; bottle-fed baby, milk and barley water. One week previously the illness began with vomiting and diarrhœa. Never very ill. Stools eight to ten in twenty-four hours; mucus, no blood. Child was sparely nourished, rachitic, had thrush. Weight was nine pounds. Stools in a day or two became homogeneous, two to four a day and child was discharged in one week. After ten days at home stools again increased in number, were muco-purulent in character and were streaked with blood. On second admission, July 27, the child showed no permanent improvement, lost in weight, went into collapse several times in spite of infusions and stimulants and died July 3.

*Diagnosis.*—Mal-nutrition. Ileo-colitis following dyspeptic diarrhœa.

No autopsy.

L. M. Clinical No. 199. Age, five weeks. Admitted July 27, 1904. Child fed from birth on condensed milk; weighed seven pounds on admission. Illness commenced two weeks before. Frequent stools, consisting of yellowish green mucus, six to ten a day, never blood-tinged. Ravenous appetite. On admission child was almost *in extremis;* very sparely nourished. Showed beading of ribs with Harrison's groove. Distended abdomen, with skin slightly cyanotic. There was little response to treatment and patient died five days after admission. Temperature varied after admission from 97°-104°. Stools from four to ten in number. They were never blood-tinged.

*Diagnosis.*—Mal-nutrition and dyspeptic diarrhœa.

No autopsy.

A. R. Clinical No. 280. Age, thirteen months. Admitted August 17, 1904. History of spinal meningitis at five months, after which time child was fed on condensed milk. Present illness commenced four weeks before admission. High fever, vomiting, purging, stools frequent, fluid, and then muco-purulent; blood-tinged after the second week. Nervous symptoms present; twitching of muscles, rolling of eyes. Nausea was a symptom throughout the illness. On admission child was in an extremely weak condition, made no response to treatment. Temperature ranged from 101.7°-104.1° and patient died August 20.

*Diagnosis.*—Ileo-colitis.

No autopsy.

B. S. Clinical No. 293. Age, six months. Admitted August 23, 1904. Child always sickly. Fed on condensed milk. Present illness dated back two months. Stools became eight to ten in twenty-four hours. Mucoid, often offensive. Fever in the afternoon. Rapid loss of weight. Child restless. During illness occasional periods of apparent improvement. Child was admitted in collapse. Pulseless, eyes sunken, gaze fixed, respiration slow, temperature 100.2°. Died two hours after admission.

*Autopsy.*—Areas of bronchial pneumonia in right lung. The whole ileum and large intestine was reddened. Peyer's patches swollen. Mucous membrane covered with a brownish-yellow membrane which stripped off with difficulty leaving bleeding surface. This membrane continued over the surface of most of the lower third of the ileum of the large intestine. Near the ileo-cecal valve and in the large intestine were occasional scattered patches of membrane, 1½ cm. in diameter. Mesenteric glands swollen.

*Diagnosis.*—Mal-nutrition; ileo-colitis, membranous.

W. D. Clinical No. 219. Age, eight months. Admitted August 1, 1904. Child had been poorly cared for from birth: fed on condensed milk. Six weeks before admission, present illness began with vomiting and frequent stools. History of fever, rapid loss of weight. Child cared for in a nursery. Fed, during illness, largely on rice water. On admission patient was sparely nourished, large head, sunken eyes, and fontanelles, rachitic chest and rather distended abdomen. Temperature on admission 101°. Pulse soft, somewhat irregular. Child was extremely ill. Stools varied from three to six in twenty-four hours; at first consisted entirely of muco-purulent material, often stained with blood. There was a gradual progressive loss of weight. After a fortnight the patient began slowly to improve, retained its nourishment better, stools became more fæcal in character, finally practically normal; child was discharged well on August 31.

*Diagnosis.*—Ileo-colitis.

Y. G. Clinical No. 244. Age, eight months. Admitted August 8, 1904. Child never ill before. Breast-fed till seven months: last month, cow's

milk. Three weeks previously, present illness commenced with diarrhœa, numerous stools, mucoid in character. No blood. High fever; little or no vomiting. On admission child was well nourished. Abdomen slightly distended; no rickets. Stools became fewer in number, mucus gradually disappeared. Child was discharged August 13, well.

*Diagnosis.*—Dyspeptic diarrhœa.

## Discussion.

*Clinical Diagnosis.*—A review of these abstracts indicates that of these fourteen cases six were suffering from dyspeptic diarrhœa; in six others there was clinical evidence often confirmed by autopsy of ileo-colitis, while in two the diagnosis of intestinal indigestion was made. In five of this series, two cases of dyspeptic diarrhœa and three of ileo-colitis, there was marked mal-nutrition antedating the acute symptoms. A well-marked pseudo-membrane was found at autopsy in one of the instances of ileo-colitis. The stigmata of rickets were marked in seven infants of this group.

*Condition on Admission.*—The condition of these children on admission was unfavorable, being definitely toxic in eight cases, five of which were more or less in collapse.

*Temperature.*—Nearly all of the children had irregular temperatures. In several the temperature was repeatedly sub-normal.

*Stools.*—The stools varied from three to twenty in twenty-four hours. All contained an excess of mucus. In five blood-stained mucopurulent material was present. The amount of blood was never large. The movements were usually fluid and rarely contained curds.

*Symptoms.*—Vomiting was noted in nine cases; in two it was excessive. Other symptoms which should be noted were marked abdominal distension in two instances, and in four others pronounced nervous symptoms without definite convulsions.

Broncho-pneumonia was found at autopsy once.

*Age.*—The age of these patients in this series varied from one to thirteen months, the average being 5.4 months. Usually the very young babies were marantic and did badly.

*Diet.*—Condensed milk formed the principal diet before admission in ten instances, while to but four, cow's milk of fair quality was given. None of the babies, even the three of about one month of age, were breast fed.

*Result.*—Of the fourteen cases seven died, five recovered and two

were improved; a mortality of 50%, equal to that of all the cases studied. Eight cases remained a week or less at the Sanitarium, three less than two weeks, and three between thirty and forty-five days.

*Season.*—Four were admitted in June, six in July and four in August. These cases represented clinically severe types of the diarrhœal disorders among the poorly-fed children of the poor. In nearly every instance the disease was well advanced before the child came under observation. Certainly our experience would indicate that this variety of the dysentery organism is often associated with a most severe intestinal derangement, and that ill-conditioned babies are the most susceptible subjects.

A representation of Group III of the dysentery organisms was not found alone in any case. It was, however, isolated from the stools of one infant (Clinical No. 29) in association with several other types discussed under "Combined Cases," D.

It will be recalled that this variety is very similar to Group II, Hiss "Y," differing only in its early fermentation of Saccharose and in its agglutinative reactions.

### *C. Cases with Flexner-Harris Type.*

The group of cases next in point of number to those associated with the "Y" type of dysentery bacilli are the instances of diarrhœa in which the Flexner-Harris variety, Group IV, was alone found in the dejecta.

The following is a summary of these histories, six in number:

M. K. Clinical No. 36. Age, twenty-one months. Admitted June 25, 1904. Child had never been sick before. Food, recently, milk and table diet. Present illness began eight weeks before. On admission had vomiting and diarrhœa. Stools never more than eight in twenty-four hours. Mucus was present at height of illness. No pus or blood. Improvement had commenced when first seen. Patient discharged well, after a week.

*Diagnosis.*—Gastro-enteritis, chronic, mild type.

E. Y. Clinical No. 111. Age, thirteen months. Admitted June 29, 1904. Previous feeding, largely proprietary foods. Present illness commenced six days before admission with diarrhœa and fever. Stools mucoid in character, contained occasional traces of blood. Child responded promptly to treatment and was discharged well in about ten days.

*Diagnosis.*—Dyspeptic diarrhœa.

D. F. Colored twin. Clinical No. 52. Age, eight months. Admitted June 28, 1904. Birth had been difficult. Child was syphilitic, bottle-fed, for most part, fresh cow's milk. Four days before admission bowels became frequent, four to six in twenty-four hours. Stools contained mucus, curds, no blood. Child was restless, had fever, but was never very acutely ill. On examination, patient was found to be fairly well nourished, but with cranio-tabes and rachitis. General popular eruption over the buttocks. Child responded slowly to treatment and was discharged well, July 23.

*Diagnosis.*—Syphilis, dyspeptic diarrhœa, chronic.

J. S. Clinical No. 126. Age, five months. Admitted July 12, 1904. Child had never been well. Fed on condensed milk from birth. Present illness began nine days before admission, with fever and diarrhœa. Stools green, mucus, never blood-tinged. Child was poorly nourished, somewhat cyanosed; pulse tension low; extremely restless. No permanent response to treatment, cyanosis continued and child died July 18.

*Autopsy.*—Hypostatic congestion of lungs with small areas of bronchopneumonia. Some fatty and parenchymatous degeneration of heart muscle and liver. There were areas of hyperemia scattered here and there in the small intestines, with moderate enlargement of Peyer's patches. About 30 cm. above the ileo-cecal valve the small intestine became suddenly thickened: its surface rough and covered with a necrotic material which stripped off with difficulty. This pseudo-membrane covered the mucosa also of the large intestine: the wall of the intestine was much thickened and the mucosa moderately congested. There was no ulceration.

*Diagnosis.*—Ileo-colitis, membranous.

L. J. Clinical No. 224. Age, sixteen months. Admitted August 3, 1904. No other previous illness. Had been fed on condensed milk. Three weeks before admission child had an attack of diarrhœa. Stools contained mucus and were occasionally blood-tinged. No history of fever, no vomiting. On admission child was found to be poorly nourished, with rickety bone-lesions. Stools were not increased in number after admission, and the child was discharged in four days, well.

*Diagnosis.*—Dyspeptic diarrhœa, convalescent.

I. L. Clinical No. 230. Age, two months, twin. Admitted August 4, 1904. Instrumental delivery. No previous history of acute illness. Child fed on condensed milk. Two weeks before admission the child was taken ill with moderate diarrhœa. Stools, six to eight in twenty-four hours, contained mucus and pus. No history of blood. On admission the child was markedly emaciated: head sutures overlapped. Pulse was small and thready. Vomiting persisted during stay at the Sanitarium. After ten days there was sudden collapse and the child died August 16. There was no elevation of temperature.

*Autopsy.*—No marked abnormality about any of the organs; in the in-

testines were occasional scattered areas of ecchymosis. Throughout the ileum and large intestines Peyer's patches were swollen and hemorrhagic. No ulceration present. Mesenteric glands moderately hypertrophied.

*Diagnosis.*—Mal-nutrition; dyspeptic diarrhœa, terminal.

### Discussion.

*Diagnosis.*—This group embraces cases of widely different clinical appearance; one a chronic gastro-intestinal disturbance in an older child who was convalescent on admission. Three were rather mild instances of acute dyspeptic diarrhœa, in another the acute symptoms were superimposed upon a long period of mal-nutrition, while in the sixth there was found at autopsy a well-marked membranous ileo-colitis.

*Stools.*—Mucus was present in all cases in the stools, which varied in number, from 3 to 12 in 24 hours. Blood was noted in but one instance, and then only an occasional fleck. There was no marked elevation of temperature. Moderate cyanosis was present in the case of membranous ileo-colitis.

*Diet.*—Four of the series had been fed on condensed milk, one on table-diet, and one on cow's milk of fair grade.

Three cases remained under treatment less than one week, two between one and two weeks and one twenty-five days.

*Age.*—In age the patients varied from 2 to 21 months, the average being 10.5 months.

*Season.*—Two cases were admitted in June, two in July and two in August.

*Result.*—Four were discharged well and two died, a mortality for the group of $33\frac{1}{3}\%$.

### *D. "Combined" Cases. More Than One Type of Bacillus Dysenteriæ Present.*

In thirteen cases of the series more than one variety of the dysentery organism were found in a single patient. These instances have been brought together under the caption, "Combined Groups." The combination of organisms found in the several cases is as follows. The numbers are the clinical numbers, which appear also in the abstracts:

*Combined Groups* of Dysentery Bacilli found in Single Cases.

a. Groups I and IV, 2 cases, Nos. 243 and 213.
b. Groups I and II, 3 cases, Nos. 97, 190 and 263.
c. Groups I, II, and IV, 2 cases, Nos. 214 and 253.
d. Groups I, II, III, IV, and B, 1 case, No. 29.
e. Groups II and IV, 5 cases, Nos. 122, 164, 193, 218 and 265.

M. H. Clinical No. 243. Age, ten months. Admitted August 8, 1904. Never ill before except for bronchitis in the winter. Fed on condensed milk for first three months, later on cow's milk. Two weeks before admission present illness began with nausea and vomiting and later, diarrhœa. Stools, eight to ten in twenty-four hours: they were mucous and often streaked with blood. Patient was never very ill. After admission temperature was never above 99.4°. Stools were blood-tinged for several days, and contained little pus. Child made a good recovery.

*Diagnosis.*—Ileo-colitis, mild.

W. B. Clinical No. 213. Age, nine months. Admitted July 29, 1904. Child fed, after third week, on condensed milk and oat-meal water. Six weeks previously patient became ill with vomiting and diarrhœa: stools, twelve to sixteen in twenty-four hours: green, mucoid, no blood noticed. Some fever and tenesmus. Since onset child has had periods of improvement followed by return of severe diarrhœa and considerable stomatitis with œdema of lower extremities. Child was restless and fretful on admission, was sparely nourished; temperature 102°. Did not respond to treatment and died August 1.

*Autopsy.*—Lower ileum found to be dark red: mucous membranes roughened. Peyer's patches swollen. Numerous small ulcers were present in the lower third of the ileum, and from this point down through the whole large intestine were scattered ulcers, usually with hemorrhagic bases and somewhat raised edges. These varied in size from 2 to 3 mm. in diameter. The wall of the large intestine was markedly hemorrhagic and in this situation ulcers were deeper than in the ileum and more punched-out in character. The mesenteric glands were moderately enlarged.

*Diagnosis.*—Ileo-colitis, ulcerative.

E. R. Clinical No. 97. Age, one year. Admitted July 8, 1904. Previous feeding both fresh and condensed milk. Present illness began ten days before admission with vomiting and frequent stools, eight to ten a day: green, and mucoid, occasionally blood-tinged; constant nausea. On admission the child was fairly well nourished with well-marked bi-lateral conjunctivitis. Moderate rosary. The temperature varied from 97° to 102°. Stools continued numerous, muco-purulent in character and often deeply tinged with blood. There was some œdema of the hands and feet.

The urine contained bacteria and pus cells. Child's condition improved for ten days then became rapidly worse and it died July 26.

*Autopsy.*—The bronchial glands were enlarged and caseous, with scattered miliary tubercles in both lungs, as well as in the liver and spleen. The small intestine showed little or no alteration to within near 15 cm. of the ileo-cecal valve when the walls of the ileum became thickened and hemorrhagic. In this portion of the ileum and throughout the large intestine were numerous ragged ulcers. The solitary follicles were swollen throughout. The mesenteric glands were large and firm. No tubercles were formed in the intestinal wall.

*Diagnosis.*—Tuberculous bronchial glands; terminal miliary tuberculosis; ileo-colitis, ulcerative.

F. A. Clinical No. 190. Age, five months. Admitted July 25, 1904. No previous illness. Diet, condensed milk. The illness commenced three weeks before admission with diarrhœa. Stools, eight to ten in twenty-four hours. In a few days they became muco-purulent in character; nearly all were blood-stained. Child lost in weight. Tenesmus was marked. No convulsions, but very restless. Physical examination negative. Patient did well for several days, then suddenly had a succession of fainting spells in which the color became ashen and the pulse almost imperceptible. Temperature rose to 104°. Diagnosis of hemorrhage was made. Child died August 4.

*Autopsy.*—Marked congestion of the lower ileum but beginning 150 cm. above the ileo-cæcal valve and extending through the large intestine were occasional losses of substance, the ulcers being independent of the follicles varying in size from 2 to 8 mm. in diameter. Several of them were bleeding. Immediately about the valve the mucosa was little altered; elsewhere it was thickened. The mesenteric glands were firm and swollen.

*Diagnosis.*—Ileo-colitis, ulcerative.

D. McC. Clinical No. 263. Age, six months. Admitted August 14, 1904. No special previous illness; occasional colic. Diet, cow's milk and Mellin's Food. Two weeks before admission present illness began with diarrhœa: stools soon became muco-purulent in character and were deeply blood-tinged. There was rapid loss of weight. Tenesmus. On admission child was drowsy, restless, with sunken fontanelle and abdomen. Rales were heard at the bases of both lungs. Mucus, blood and pus continued in the stools, the patient remained listless and died on the fourth day after admission.

*Autopsy.*—Beginning about 39 cm. above the ileo-cæcal valve and extending throughout the whole large intestine the intestinal wall was markedly thickened, the mucosa roughened and congested. Peyer's patches were swollen, and numerous irregular ulcers, many of them with bleeding bases, were present in the colon and rectum. The lymphatic glands were swollen.

*Diagnosis.*—Ileo-colitis, ulcerative.

L. A. Clinical No. 214. Age, two and one-half years. Admitted July 30, 1904. Child's general health fair except for grippe the previous winter. Six days before admission present illness commenced with high fever and diarrhœa. Stools putrid in odor, ten to thirty a day, and deeply blood-stained; three days after onset of acute symptoms, considerable vomiting. On examination, the child was rather poorly nourished, no signs of rickets; chest and abdomen negative. Pus and blood remained in the stools for several days after admission. These movements gradually became fewer in number and fecal in character. The child's general condition improved and it was discharged well, August 19.

*Diagnosis.*—Mal-nutrition; ileo-colitis, ulcerative.

J. B. Clinical No. 253. Age, two years. Admitted August 10, 1904. Child previously had been fairly well, fed on table diet. Three weeks before was taken ill with vomiting and diarrhœa. Stools at first mucoid, then, after ten days of improvement in patient's general condition, they became deeply blood-tinged. On admission, the child was markedly emaciated, eyes sunken, abdomen scaphoid and rickets. After admission there was marked restlessness and tenesmus, frequent vomiting, pulse rapid, thready in character. Temperature did not rise above 100.4°. Blood was constantly present in the stools. Died August 13.

*Autopsy.*—The upper ileum was apparently normal: at about 300 cm. above the ileo-cecal valve the mucous membrane of the bowel became roughened and the wall thickened. There were scattered areas of hemorrhage. The mucosa was markedly thickened throughout the whole large intestine and numerous small ulcers were present. Many of the solitary follicles had bleeding bases. Mesenteric glands were large and firm.

*Diagnosis.*—Ileo-colitis, ulcerative.

J. O'N. Clinical No. 29. Age, four months. Admitted June 24, 1904. Child poorly nourished; fed on condensed milk. Five days before admission was seized with vomiting followed by diarrhœa. Stools not more than four to six in twenty-four hours; mucous, no blood. Considerable abdominal pain. Patient was admitted in semi-comatose condition, could not be aroused. Pulse weak and rapid. Lungs clear. Extensive thrush in mouth. For a day or two there was some response to treatment, later Cheyne-Stokes breathing, convulsive twitchings and death three days after admission. Temperature during observation, 98.2°-102°.

No autopsy.

*Diagnosis.*—Mal-nutrition, dyspeptic diarrhœa.

C. H. Clinical No. 122. Age, nine months. Admitted July 11, 1904. Previous condition of child was fairly healthy. Diet, cow's milk and water. Two weeks before admission present illness commenced with increasing drowsiness followed by diarrhœa. Stools four to six a day, mucoid in character, at that time not blood-tinged. No vomiting, little or no

fever, continued loss of weight. On examination the child was found to be pale and fretful; markedly rachitic. Stools after admission were ten to sixteen in twenty-four hours, for the most part muco-purulent; deeply blood-tinged. Temperature varied from 99°-100°. There was marked tenesmus and considerable loss of weight. After a protracted illness the condition of the bowels gradually improved, appetite returned and child was discharged August 20, improved.

*Diagnosis.*—Ileo-colitis; mal-nutrition.

F. L. Clinical No. 164. Age, seven months. Admitted July 19, 1904. No previous illness. Diet, condensed milk. Two weeks before admission child was taken suddenly ill with vomiting, diarrhœa and fever. Stools, six to eight a day, contained mucus; no blood. Child improved under treatment at the Johns Hopkins Hospital Dispensary, but suffered a relapse and when admitted to the Sanitarium was pale and restless, with depressed fontanelle, scaphoid abdomen and feeble pulse. For a few days the child improved; stools, however, continued muco-purulent, often blood-tinged and varied from ten to fifteen in twenty-four hours. Temperature remained constantly over 100°, occasionally rising to 104°. Child gradually grew weaker and died July 29.

No autopsy.

*Diagnosis.*—Ileo-colitis.

D. K. Clinical No. 193. Age, thirteen months. Admitted July 26, 1904. Child was never robust; fed on cow's milk and water, and lately, table-diet. Six weeks before admission present illness began with high fever, occasional vomiting and diarrhœa. Stools, eight to fifteen in twenty-four hours. Child became better. After a season of intense heat in the city, again grew worse and blood appeared in the stools. With this relapse there was considerable tenesmus. On examination the child was found to be fairly well nourished. Stools muco-purulent and blood-tinged. After a few days there was rapid improvement. Child discharged well on August 12. Little or no fever while at the Sanitarium.

*Diagnosis.*—Ileo-colitis.

F. H. Clinical No. 218. Age, fifteen months. Admitted August 1, 1904. Child always delicate. Had been fed largely on condensed milk. Two weeks before admission moderate diarrhœa set in. Stools, four to six in twenty-four hours, later, twelve to sixteen. There was no vomiting, no history of blood in stools; however, they contained mucus and were green in color. There was moderate fever. Child was sparely nourished; moderately rachitic. Consolidation made out in both apices and numerous moist rales throughout both lungs. Posterior cervical glands upon the right side considerably enlarged. Patient lost rapidly. During observation the stools became muco-purulent, often streaked with blood. The child died August 17.

*Autopsy.*—The apex of each lung contained a small area of consolidation, and throughout both lungs there were numerous miliary tubercles. Several of the bronchial glands were enlarged and caseous. Occasional miliary tubercles were found in the liver and spleen. The small intestine was apparently normal till about 150 cm. above the ileo-cecal valve, where there was a deep punched-out ulcer with overhanging mucosa. On the peritoneal surface corresponding to the ulcer were several miliary tubercles. Single ulcers were scattered here and there throughout the large intestine. Mesenteric glands were everywhere enlarged, caseous and found near a fibrous capsule.

*Diagnosis.*—Ileo-colitis; tuberculous and dysenteric. Pulmonary tuberculosis with miliary tuberculosis of the liver, spleen, and mesentery.

J. L. Clinical No. 265. Age, four months. Admitted August 15, 1904. Child was not strong. Diet since birth, condensed milk. Six weeks before patient was admitted to Sanitarium because of an apparently mild attack of dyspeptic diarrhœa. He quickly responded to treatment and was discharged well July 13. After three weeks of its usual health the child suddenly became worse. The stools again mucous six to eight in twenty-four hours; no history of blood. The patient was admitted after one week in marked collapse. Pulse weak and rapid, skin cool, eyes sunken. Temperature 99°. There was but slight response to vigorous stimulation. The stools were muco-purulent, often blood-tinged and eight to twelve in twenty-four hours. The child gradually lost strength and died August 19.

*Autopsy.*—There was moderate congestion of the organs; lungs were clear; bronchial glands were not enlarged. No abnormalities were found in the stomach and upper ileum, the mucosa being pale. About 50 cm. above the ileo-cecal valve and extending to the large intestine were several small punched-out ulcers surrounded by thickened and reddened mucosa. The mucous membrane of the large intestine was thickened and hemorrhagic throughout, the follicles were prominent, the mesenteric glands enlarged.

*Diagnosis.*—Ileo-colitis, ulcerative.

## Discussion.

A résumé of these cases shows them to be of a more serious nature than the average of the whole series.

*Diagnosis.*—In twelve of the thirteen cases the diagnosis of ileo-colitis was made. In but one was there no indication before or after death of marked inflammatory alteration of the intestinal wall. Here an acute dyspeptic diarrhœa occurred in a marantic infant.

Tuberculosis was present in two instances, in one as miliary tuberculosis arising from an old caseous bronchial gland, in the other there was an extensive involvement of both lungs with cavity formation and

several typical tuberculous ulcers in the intestines. Here was apparently an infection of the intestinal wall with the dysentery organism of both the "Y" and Harris type as well as the tubercle bacillus.

*Ante mortem.*—In eight of the twelve cases of the ileo-colitis there was evidence of ulceration of the intestine.

At least one fatal case followed a mild and apparently cured case of dyspeptic diarrhœa.

*Condition.*—The general condition of but one baby in this group was considered good on admission; four were thought to be in fair condition: four were in a state of pronounced mal-nutrition, and four in definite collapse.

*Temperature.*—The highest temperature reached was 104°—the lowest 97°. In general these cases had afterwards a less febrile course than the groups heretofore discussed.

*Stools.*—The stools varied in number from 4 to 20 in 24 hours. They all contained mucus. Pus was present usually in considerable quantities in eleven instances; blood was noticed repeatedly also in eleven cases.

The case showing tuberculous ulceration of the intestines at autopsy passed during life mucous stools without microscopic blood or pus.

*Other Symptoms.*—Vomiting, although noted in nine of the cases, was not a marked feature in any of these patients.

Tenesmus was troublesome in three of the infants, and severe nervousness in two.

Pyelitis was a complication in one instance. Thrush was once noted.

*Feeding.*—Condensed milk had formed the chief diet antecedent to the illness in eight of the babies. Three were fed at the table, and but two were given cow's milk of fair quality.

Eight of the patients were rachitic.

The length of stay at the Sanitarium was considerably longer for the other groups, but five infants remained less than a week, three between one and two weeks; the longest stay being forty days.

*Age.*—The youngest infant treated was a month old, the oldest, 30 months, the average age time being 11½ months.

*Season.*—The season of the year was somewhat later than for the other groups, but one case was admitted in June, five in July and seven in August. This is in line with clinical experience that the se-

vere ulcerative cases are more apt to occur, in the second half of the summer, frequently after an attack of dyspeptic diarrhœa.

The death rate was large—nine of the infants, or 69%, died, three recovered and one was improved. These results were to be expected in cases of ileo-colitis admitted late in the course of the disease.

Autopsies were obtained in seven of the nine fatal cases. In all seven, more or less extensive ulcerative ileo-colitis was found.

*E. Cases with Dysentery Bacilli of an Undetermined Type.*

In the following three cases, the abstracts of which follow, organisms belonging to the dysentery group were isolated, but the type to which they belonged was not determined before the culture died out.

L. McG. Clinical No. 159. Age, one month. Admitted July 18, 1904. Never sick before. Diet, after twelfth day, cow's milk and water. Present illness began one week previously, with vomiting and diarrhœa. Stools, twelve to eighteen in twenty-four hours, contained much mucus; considerable colic. Child rather weak on admission, restless. Abdomen somewhat distended. Child did well, stools became fecal in character, and was discharged July 30, well.

*Diagnosis.*—Dyspeptic diarrhœa.

A. R. Clinical No. 177. Age, eighteen months. Admitted July 21, 1904. Never ill before. Table diet. Four days before admission present illness began with diarrhœa. Stools, twenty to thirty in twenty-four hours, contained considerable mucus, often blood-tinged. Patient had high fever, Appetite poor. On examination child was fairly well nourished. Stools were muco-purulent in character, often blood-tinged, four to eight in twenty-four hours. They improved under treatment, became fecal in character and the child was discharged July 28, well. Temperature did not rise above 100°, while under observation.

*Diagnosis.*—Ileo-colitis; ulcerative.

L. S. Clinical No. 192. Age, two months. Admitted July 25, 1904. One of twins. Never ill before. Fed on condensed milk. Three days before admission appetite failed and stools increased in frequency and became green in color. Child was small, but well formed. Stools on admission six to ten, grass green, mucoid; contained considerable fecal material but no blood. There was considerable vomiting during illness. After a fortnight patient began to improve and was discharged well, August 30.

*Diagnosis.*—Dyspeptic diarrhœa; intestinal indigestion.

## Discussion.

*Diagnosis.*—These were all fairly mild, two were instances of dyspeptic diarrhœa, and one of ileo-colitis.

*Condition.*—They were admitted to the Sanitarium in fair condition. There was little elevation of temperature.

*Stools.*—The stools were mucoid in character. Blood and pus were present in one case.

The onset was marked by vomiting in two instances; one baby had a convulsion. One patient had been fed on condensed milk, one on a table diet, and one on cow's milk of fair quality.

The children remained in the Sanitarium 7, 12, and 35 days respectively. One patient was 1 month old, one 2, and the third 18 months of age. They were all admitted in July and discharged well.

### *F. Cases with Bacillus "B," "Dysentery-like" Group.*

There were but two instances in our series in which the variety of pathogenic organism found corresponded to the type "B," called by Torrey "Dysentery-like bacilli."

The abstracts are as follows:

L. S. Clinical No. 41. Age, nine months. Admitted June 25, 1904. History of pneumonia at two weeks, otherwise well. Fed on cow's milk and water. Three days before admission bowels became loose, child feverish; there was frequent vomiting, stools were offensive and fluid contained little or no blood and but little mucus. Physical examination, negative. Stools were mucous but never blood-tinged while at Sanitarium. Temperature ranged from 98°-101°. Child was discharged July 3, improved.

*Diagnosis.*—Dyspeptic diarrhœa.

J. C. Clinical No. 196. Age, six months. Admitted July 27, 1904. Previous diet, malted milk and Mellin's Food. No serious illness until three weeks before when the child began vomiting curdled milk; this was followed by frequent stools, fifteen to twenty a day, watery in character but contained mucus, no blood. There was continuous fever and three days before admission a severe general convulsion. Patient was admitted in a collapsed condition, cyanosed, dyspnœic; pulse weak and thready; temperature 104.2°. There was no response to treatment, and child died in half an hour.

No autopsy.

*Diagnosis.*—Dyspeptic diarrhœa, (severe).

### Discussion.

*Clinical Diagnosis.*—These cases represent markedly different grades of dyspeptic diarrhœa, one of a mild, the other of a severe type. The first case was only moderately ill and was discharged "improved"

in 8 days; the second was admitted in collapse after three weeks of illness with a temperature of 104°, with a history of 15 to 20 fluid mucous stools a day, and a general convulsion 3 days previously. The child was markedly cyanosed and died one-half hour after admission. The first case was seen in June, the second in July.

*Diet.*—The previous diet had been cow's milk of fair quality in the first instance, while the fatal case had been fed on a proprietary food.

### *G. Cases with Dysentery Bacilli and Streptococci.*

In the following group, eleven in number, pathogenic streptococci were isolated in connection with some type of the dysentery bacillus.

E. Y. Clinical No. 42. Age, two and one-half years. Admitted June 24, 1904. Never ill before. Table diet. Three days previously present illness began with fever, loss of appetite and diarrhœa. Mother said stools contained "corruption" and blood; about twenty in twenty-four hours. Considerable fever, especially at night. After admission child made uninterrupted convalescence, stools became fecal and child was discharged July 7, well.

*Diagnosis.*—Ileo-colitis.

A. V. Clinical No. 39. Age, four months. Admitted June 25, 1904. Child was never strong, but had been well cared for. Diet, cow's milk and water. Illness commenced one week before admission with soft, fecal stools, which were somewhat increased in frequency. One day before admission, stools became more numerous, fifteen to twenty in twenty-four hours, contained some mucus, occasionally stained with blood. Little or no nausea. High fever was present from onset. On examination child seemed rachitic. Temperature 103°. Was fairly well nourished. Child was given boiled water and was irrigated several times each day. Temperature, however, remained high and on the second day patient had several convulsions which were relieved with considerable difficulty. There was no permanent improvement and the child died June 28. The temperature had varied 100°-105.5° during the stay at the Sanitarium.

*Autopsy.*—Intestines were pale throughout, excepting for occasional scattered areas of hemorrhage. The Peyer's patches of the solitary follicles were moderately enlarged. There was no loss of substance. Pronounced hypertrophy of mesenteric glands, particularly in the region of the ileo-cecal valve. Small area of bronchial pneumonia in the right lung.

*Diagnosis.*—Dyspeptic diarrhœa, acute, toxic. Broncho-pneumonia.

B. H. Clinical No. 46 Age, twenty-two months. Admitted June 7. Never ill before. Nursed until one year of age, since then fed on cow's milk and table diet. Five days before admission present illness began

with vomiting and diarrhœa; for a few days previous to this, however, the child was dull and "droopy"; shortly after the vomiting, the stools became numerous, twenty to thirty in twenty-four hours, green, contained much mucus, soon streaked with blood. History of "high fever and severe vomiting spells." Considerable colic. Child was found to be fairly well nourished; slight rosary. Examination of chest and abdomen, negative. Temperature on admission 101°, which fell the following day to 98°, and did not at any time afterwards rise above normal. While at the Sanitarium the stools were never more than seven in twenty-four hours, but were usually muco-purulent in character, often blood-tinged. The child improved under treatment, and was discharged at parents' request before stools became perfectly normal, improved.

*Diagnosis.*—Ileo-colitis.

W. C. Clinical No. 58. Age, eight months. Admitted June 30, 1904 Fed on milk and numerous articles from the table. Seven days previously child was taken ill with high fever and loose bowels. Shortly afterwards stools became thin and child was restless and lost considerably in weight. On admission child was listless and pale. Anterior fontanelle depressed; pupils moderately contracted. Pulse small, rapid, regular. While at the Sanitarium stools were muco-purulent in character, and blood-tinged, eight to ten in twenty-four hours. Temperature did not rise above 100°. Patient lost rapidly in strength and died July 9.

No autopsy.

*Diagnosis.*—Ileo-colitis.

M. H. Clinical No. 62. Age, five months. Admitted June 30, 1904. Little was known about the child's past history. Fed on condensed milk. Stools had been frequent for several weeks before admission. On examination child was fairly developed. Stools occasionally contained green mucus, varied from two to six in twenty-four hours, no blood. Often the stools were fecal in character. There was often excessive gastric irritability. The patient remained nearly two months at the Sanitarium during which time periods of improvement were interrupted by severe attacks of vomiting. The stools frequently contained mucus, but were not markedly increased in number. There was no fever. The infant was discharged improved August 21.

*Diagnosis.*—Indigestion; mal-nutrition.

H. R. Clinical No. 76. Age, eight months. Admitted July 2, 1904. Patient had marasmus at three months, never completely recovered. Had been fed largely on condensed milk. Four days before admission mother first noticed acute symptoms, fever, vomiting and diarrhœa. The stools were first fecal, somewhat mucoid, four to six in number in twenty-four hours. Was treated at the Johns Hopkins Hospital Dispensary. Child was admitted in a markedly toxic condition, pale, listless; temperature 103°.

Temperature remained markedly elevated, ranging from 102°-106° the first four or five days, then gradually fell to about 100°. General condition also slightly improved, but the stools continued for the most part, mucoid and were occasionally blood-tinged. Child gradually lost in weight. Case was complicated by a persistent pyuria. Urine contained also hyalin casts and numerous colon bacilli. Specific gravity was about 1000.3. The child died August 9. During the last week of its illness temperature again became irregular, ranging from 97°-103°.

*Autopsy.*—A bronchial gland on left side was found to be enlarged and caseous. Over the corresponding pleura were scattered tubercles varying in size from 1 to 5 mm. The right lung was apparently unaffected. Moderate fatty degeneration of liver. The kidneys were congested, striations prominent; cortex somewhat thickened. Well marked cloudy swelling. The mucous membrane of the kidney, the ureters and bladder reddened and somewhat thickened. Moderate adhesive peritonitis, particularly about the appendix and large intestine. On section the upper portion of the small intestine was found somewhat congested, and at a point 50 cm. above the ileo-cecal valve, mucosa became thickened and covered with a dirty-brown material which stripped off, leaving a bleeding surface; the whole lower intestinal tract was deeply congested. Mesenteric glands enlarged and firm.

*Diagnosis.*—Ileo-colitis, membranous; pyelo-nephritis; tuberculous bronchial glands; tuberculous pleurisy.

L. R. Clinical No. 114. Age, five months. Admitted July 8, 1904. Child never robust. Fed, for most part after two weeks, on condensed milk. One week before admission, present illness began with moderate diarrhœa; stools, five to eight in twenty-four hours, first fecal and lumpy, later mucoid in character. No history of blood. Little elevation of temperature, but markedly drowsy almost from onset. Rapid loss in weight. Child was admitted in a weak condition, pulse small; somewhat difficult to arouse the patient. Shorty after admission patient went into collapse, failed to respond to stimulation, became cyanotic and died July 10.

*Autopsy.*—Moderate congestion of all organs, but little abnormality noticed in stomach and small intestines except that Peyer's patches were enlarged throughout. Mucous membrane of large intestine, particularly near the cæcum, moderately hemorrhagic, but no definite ulceration was present. The solitary follicles were prominent. Mesenteric glands were everywhere enlarged and firm, often hemorrhagic.

*Diagnosis.*—Mal-nutrition; dyspeptic diarrhœa, severe.

L. T. Clinical No. 139. Age, six months. Admitted July 14, 1904. Child always been sickly, "vomiting spells." Fed after second week on condensed milk. One day before admission was taken acutely ill with diarrhœa, stools green, mucoid; one on second day of illness, blood-tinged. Some vomiting, restless, feverish, no convulsions. Child was markedly

toxic on admission. Patient had all the stigmata of rickets. Breath sounds were harsh, not blowing in character. Thrush was present in mouth. Temperature on admission 99°. There was no response to prompt, vigorous treatment. 150 cc. of anti-dysentery serum was given in twenty-four hours. The stools were numerous, often blood-tinged. Child died July 16.

*Autopsy.*—Scattered areas of bronchial pneumonia were found in both lower lobes. Liver was congested and fatty. Stomach was filled with about 10 cc. of dark brown fluid similar to the vomitus. In the small intestines were extensive scattered areas of hemorrhage; Peyer's patches were congested and enlarged. The lumen of the large intestine contained a large amount of bloody fluid; the mucous membrane was everywhere congested, and here and there in the wall of the large bowel there was slight irregular ulceration of the membrane. The mesenteric glands were all large and firm.

*Diagnosis.*—Mal-nutrition; ileo-colitis, ulcerative, and toxic.

R. G. Clinical No. 178. Age, eight months. Admitted July 21, 1904. Child had been sickly most of its life. Fed on store milk and table-diet. Two weeks before admission symptoms became acute. Stools, eight to ten in number. Considerable vomiting. Child became drowsy, lost rapidly in weight. No blood was noticed in the stools. On admission child was sparely nourished, markedly rachitic, eyes sunken, restless. Abdomen, scaphoid. Child's condition gradually became worse, there was almost constant nausea. Stools, during stay at the Sanitarium, were muco-purulent and occasionally blood-tinged. Child died July 25.

*Autopsy.*—Ileum thickened, beginning about 150 cm. above the ileo-cecal valve. From this point on there were scattered areas of hemorrhage continuing almost down to the large intestine. Mucosa was roughened and red; Peyer's patches usually swollen, solitary follicles enlarged. Scattered ulcers were present on the colon. Several small vessels apparently had ruptured into the lumen of the gut. Liver was markedly fatty.

*Diagnosis.*—Mal-nutrition; ileo-colitis, ulcerative.

R. P. Clinical No. 113. Age six months. Admitted July 9, 1904. Child had been well excepting for occasional attacks of bronchitis in the winter. Had been carefully fed on milk and barley-water. Two weeks before admission, present illness began with loose bowels and diarrhœa. Stools, six to eight in twenty-four hours, green, mucoid; no blood. Considerable tenesmus. Child was well developed. Physical examination, negative. Stools, soon after admission, two to four in twenty-four hours, green, occasionally, but were largely fecal and never blood-tinged. Child responded slowly to treatment, and gradually improved, and was discharged well, August 10.

*Diagnosis.*—Dyspeptic diarrhœa; chronic intestinal indigestion.

A. H. Clinical No. 238. Age, four months. Admitted August 6, 1904. Child never robust. Fed on cow's milk of inferior quality. Six days before admission bowels became loose, stools watery, contained mucus, four to six in twenty-four hours. No history of blood; no vomiting. For the last two or three days the child was said to be drowsy. Some swelling noticed of lower extremities, no convulsions; considerable loss of weight. On examination, child found to be sparely nourished; sunken fontanelles; tongue coated. Rachitic rosary, Harrison's groove. Chest was clear; abdomen markedly extended. Child seemed fairly comfortable throughout the first night after admission, but in the morning collapsed, respirations became rapid, Cheyne-Stokes in character, no response to stimulation and child died August 7. Temperature during admission varied from 101.2°-101°. Stools contained no blood.

*Autopsy.*—Œdema of hands and feet. Slight increased amount of fluid in the peritoneal cavity. Moderate hypostatic congestion at the base of both lungs. Heart valves delicate; heart muscles good color. Liver slightly fatty. The stomach and small intestine showed little alteration, mucous membrane being smooth, but not congested, until about 30 cm. above the ileo-cecal valve the intestinal wall became thickened and slightly hemorrhagic. This thickening of the intestinal mucosa continued throughout the whole of the large intestine; in addition, there are small scattered areas of hemorrhage and enlargement of solitary follicles. There was considerable blood-stained fluid in the lumen of the large intestine; no definite loss of substance. The mesenteric glands were somewhat enlarged and firm; the peritoneum, particularly about the sigmoid flexure, was markedly œdematous. This gelatinous condition is especially associated with the portion of the gut showing most pathological alteration. Retro-peritoneal glands not enlarged.

*Diagnosis.*—Ileo-colitis, toxic; œdema of the mesentery.

## Discussion.

*Diagnosis.*—Of the cases above cited, three belonged to the toxic and seven to the inflammatory form, ileo-colitis, of diarrhœal disorders, and one was more properly classed as indigestion.

Mal-nutrition was a prominent feature in four cases.

One case of dyspeptic diarrhœa was complicated by broncho-pneumonia, and one of ileo-colitis by pyelo-nephritis and tuberculous pleurisy. The small intestine of the last case showed at autopsy a well-marked pseudo-membrane.

*Condition.*—Three of the infants were admitted in collapse and but one in really good condition.

There was no high fever except in the cases of broncho-pneumonia and tuberculous pleurisy.

*Stools.*—The number and character of the stools did not differ from those of the other groups. All of the movements were mucoid; muco-purulent material was noted in six cases, and more or less blood also in six.

Vomiting was marked in two instances. Several were drowsy and restless; one had convulsions at onset.

*Diet.*—Four had been fed on condensed milk, three on table-diet and three on cow's milk, in two instances of fair, and in one of bad quality. The stigmata of rickets were prominent in two infants.

One-half of the cases remained less than a week at the Sanitarium, three between one and two weeks, and three longer, the longest stay being 53 days.

*Age.*—Seven of the patients were 6 months or younger, the oldest being 30 months. The average age was 10 months.

*Season.*—Three babies were admitted in June, seven in July and one in August.

Seven cases resulted fatally,—a mortality of 63.06%.

Two babies recovered and two were discharged improved.

It would seem that the intestinal infection of the streptococci together with dysentery bacilli was a combination exceedingly dangerous for infants.

### *H. Cases with Streptococci Alone.*

In the next group of cases, six in number, streptococci were the only pathogenic organisms found. No dysentery bacilli of any of the various types referred to were isolated from the stools at autopsy, although in all cases careful and repeated search was made.

E. R. Clinical No. 3. Age, six months. Admitted June 6, 1904. Child never well, always had poor digestion. Pneumonia two months before. Fed on boiled cow's milk. Present illness began four weeks before, with vomiting and diarrhœa. Stools, at first, six to ten a day, green, mucoid, no lumps; blood was noticed for first time, ten days before admission; since then many of the stools have been blood-stained. One week before admission vomitus contained bright red blood; this was noticed daily afterwards. There was considerable loss in weight, little or no fever. On admission the child was well developed, fairly well nourished. Chest and abdomen, negative. Anterior fontanelle slightly depressed. Patient had a long illness at the Sanitarium; stools persistently contained blood, sometimes in considerable quantity. There was no fever; child continued to lose in weight, stools became muco-purulent in character. There was oc-

casional temporary improvement, but on the whole there was a gradual loss of strength and the child died on July 4. A partial autopsy only was allowed.

*Autopsy.*—In the mucous membrane of the stomach were numerous hemorrhagic areas, in the center of which were several small crater-like depressions, possibly ulcers. Similar depressions were also found in the duodenum. Beginning at a distance of 200 cc. above the ileo-cecal valve there were several small ulcers, 2 mm. in diameter, with smooth elevated edges and red and bleeding hemorrhagic bases. From this point towards the large intestine these ulcers increased in number. Most of them were irregular in outline and have no definite relation to the long diameter of the intestine; 15 cm. above the ileo-cecal valve the ulcers stop abruptly. The large intestine contained areas of moderate hemorrnage, but there was no loss of substance. Solitary follicles were enlarged, mesenteric glands were large and reddish in color; other organs not removed, apparently normal.

*Diagnosis.*—Ileo-colitis, ulcerative.

E. W. Clinical No. 30. Age, four months. Admitted June 24, 1904. Child had never been robust. Had been fed on milk of inferior quality, variously diluted. Eleven days before admission child was taken ill, vomiting sour milk, followed by diarrhœa, numerous stools, watery, and contained mucus; no history of blood. Child lost rapidly in weight during illness. On examination child was found to be sparely nourished; depressed fontanelle; abdomen not distended. After a few days acute symptoms subsided and stools became fecal; the weight, however, continued to decrease and the case assumed a marantic type. After a long illness on various diets, the child died, extremely emaciated, but with normal stools.

*Autopsy.*—Marked atrophy of all musculature of the body; little or no sub-cutaneous fat. The wall of the small intestine somewhat thickened and in places hemorrhagic. There was no definite loss of substance; the Peyer's patches were moderately enlarged; solitary follicles were prominent. Mesenteric glands slightly hypertrophied, except in the scattered areas of injection the mucosa of the intestine was pale.

*Diagnosis.*—Marasmus; dyspeptic diarrhœa.

A. K. Clinical No. 93. Age, four and one-half months. Admitted July 7, 1904. There had been no previous admission, present illness began with vomiting sour curds followed by diarrhœal stools, eighteen to twenty in twenty-four hours; contained mucus, no blood. Child was feverish and fretful; no convulsions; rapid loss of weight. Patient was found to be sparely nourished, with moderately depressed fontanelle, slightly rachitic. Admitted in moderately toxic condition. Temperature 103.4°. Child improved slowly for the first few days of admission and temperature became normal on the fourth day. There was considerable difficulty in returning to a milk diet. Child discharged at parents' request, July 20, improved.

*Diagnosis.*—Dyspeptic diarrhœa, acute.

C. S. Clinical No. 170. Age, three months. Admitted July 21, 1904. Child was well until June 27, when he was admitted to the Sanitarium with a mild attack of dyspeptic diarrhœa, and was discharged well, June 8. Previous diet, condensed milk. After a fortnight, during which the child seemed to the mother perfectly well, he was taken ill again five days before admission, with vomiting and diarrhœa, and fever. Stools, mucoid, but not blood-stained. Condition on admission was fairly good. Chest and abdomen, negative. Temperature 98.2°-98.6°. Responded fairly well to treatment. Discharged at parents' request while the stools were slightly mucoid in character, improved.

*Diagnosis.*—Dyspeptic diarrhœa.

E. R. Clinical No. 179. Age, three months. Admitted July 22, 1904. Never ill before. Child exclusively breast-fed. Four days before admission bowels became loose and there was slight nausea and vomiting. Stools, eight to ten a day, green, mucoid in character, never blood-tinged, no tenesmus. Child's appetite remained good. Mother thought there was no loss in weight. Slight fever. Child was found to be well nourished; abdomen slightly distended. Physical examination, negative. Responded well to treatment; temperature dropped from 101.2° on admission to normal. Was discharged well, July 26.

*Diagnosis.*—Dyspeptic diarrhœa.

M. K. Clinical No. 212. Age, six months. Admitted July 27. Previous diet, condensed milk. Child became ill three months previously. Attacks of diarrhœa, alternating with periods of constipation, also associated with vomiting. Had lost weight extensively. Patient became restless and hard to arouse. Mucus was present in the stools, but no blood. Child was found listless, sparely nourished, rachitic. Extremities rather cool. Stools were largely fecal in character, often lumpy; contained mucus, no blood. No elevation of temperature. Child improved somewhat after a long period, and was discharged improved, August 31.

*Diagnosis.*—Indigestion.

## Discussion.

*Diagnosis.*—Rather in contrast to the groups before cited but one of these cases could be called ileo-colitis. In this one there were numerous ulcers in the lower ileum but none in the large intestine, the walls of which, however, were thickened and in places hemorrhagic. In the remaining patients there was no evidence of inflammation of the intestinal wall. One was a chronic case in which mal-nutrition dominated the clinical picture, two were instances of acute dyspeptic diarrhœa, another was a relapse after dyspeptic diarrhœa, and the remaining patient had a rather intestinal indigestion.

*Condition.*—Three of the cases were more or less marantic on admission, two were in fair and one in good condition. With the exception of one infant none had much elevation of temperature.

*Stools.*—In this patient the number of the movements reached 20 in 24 hours; in the others never more than 10. Blood and pus in addition to the mucus were present in but one case. Vomiting was noted in all cases; it was never excessive. In the instance of ileo-colitis the vomitus frequently contained blood.

One baby, the one with prolonged indigestion, suffered from a chronically infected knee with discharging sinuses. There was no definite evidence of tuberculosis.

*Diet.*—Three of the patients had been previously fed on condensed milk, one was breast fed, and two were given cow's milk, one of bad and the other of fair quality.

But two of the infants left the Sanitarium in less than a week; the others remained three weeks or longer.

*Age.*—All the patients were young—under 7 months of age—the youngest being 3 months.

*Season.*—Two were admitted in June, three in July, and one in August.

*Result.*—Two cases resulted fatally, including the one of ileo-colitis, one completely recovered and three were discharged improved.

This limited number of observations would indicate that the presence of streptococci in the stools may not necessarily involve a grave prognosis, and that such an infection is less severe than when streptococci are present in association with dysentery bacilli. Indeed streptococci have been found not infrequently in normal stools.

### *I. Cases with Organisms Other Than Dysentery Bacilli and Streptococci.*

A small group of five cases is added in which organisms other than dysentery bacilli and streptococci, but which agglutinated with the patient's blood and were pathogenic (except case No. 170) for laboratory animals, were isolated from the stools. In the stools of all these infants every effort was made to find dysentery organisms.

The findings in these cases were as follows:

Cases 17 and 64.—Bacillus coli communis (pathogenic).

Cases 11 and 120.—Bacillus pyocyaneus (pathogenic).

Case 170.—Bacillus pyocyaneus (non-pathogenic).

F. P. Clinical No. 11. Age, ten months. Admitted June 13, 1904. Nursed at the breast until five months of age; since then fed on diluted cow's milk. Never ill before; general health fairly good until six weeks ago when the child is said to have had pneumonia, and was very ill for four weeks. Did not regain strength; lost considerably in weight; fretful; tendency to be constipated; stools normal in appearance and consistency. Eczema has persisted on the face for several weeks. Child came to Sanitarium because of lack of appetite and loss of weight. On examination patient was found to be well nourished, with marked weeping eczema about the right ear, and papular eczema about the face. Chest and abdomen negative. Child improved rapidly at the Sanitarium; the stools contained slight amount of mucus, never more than four in twenty-four hours, became homogeneous and brown in color. Child discharged well June 26. No elevation in temperature.

*Diagnosis.*—Indigestion; eczema.

I. W. Clinical No. 17. Age, eight months. Admitted June 16, 1904. Fed exclusively on breast until two weeks previously; since then on modified milk with Mellin's Food. During early infancy the child was thought by its mother to be pale. Three days ago the present illness began with intense vomiting, accompanied by abdominal pain, followed by diarrhœa; four to six stools in twenty-four hours, green, mucoid. Child was found to be well nourished, moderately anemic. Curious smooth bosses, in diameter 1-2 cm. and raised ½ cm. above the scalp level, were present on the skull. No cranio-tabes. No glandular enlargement. No elevation of temperature. Patient did well at the Sanitarium, responded promptly to modification of diet. The stools at first contained a small amount of mucus which disappeared in a few days, and child was discharged well, June 26. Blood count showed four million red blood corpuscles.

*Diagnosis.*—Gastro-intestinal indigestion.

H. W. Clinical No. 64. Age, six months. Admitted June 30, 1904. Child had never been ill before; nursed at the breast for three months. Diet had been diluted cow's milk. Three days before admission present illness began with nausea and vomiting, followed by frequent stools which were green, mucoid in character and contained curds. Temperature at onset, 102.5°. On admission child was found to be well nourished; tongue coated. Chest and abdomen negative. Temperature 102.8°. Child improved slowly after admission; temperature became normal on third day. Stools after tenth day were homogeneous and semi-formed, and child was discharged well, July 17.

*Diagnosis.*—Dyspeptic diarrhœa.

C. S. Clinical No. 170. Age three months. Admitted July 21, 1904. Patient was a rather frail infant; fed largely on condensed milk. It was admitted about a week after the onset of the acute symptoms, which began with vomiting, diarrhœa and fever. The stools, six to ten in twenty-four hours, were mucoid, never blood-stained or purulent and there was but

slight elevation of temperature while under observation. The baby did fairly well at the Sanitarium and was discharged improved July 27.

*Diagnosis.*—Dyspeptic diarrhœa.

G. S. Clinical No. 120. Age, six months. Admitted July 11, 1904. Child never robust; fed exclusively on condensed milk almost from birth. Two weeks before child became acutely ill, vomited frequently and in large amounts. Stools, ten to twelve a day, green, mucoid, no history of blood; high fever. For the two days before admission, apparently following medicine, there had been no movements of the bowels. Child was admitted in collapsed condition, bladder distended, readily palpable. Deep corneal ulceration in both eyes, with conjunctivitis of high grade. Chest and abdomen were negative. Urine contained a few hyalin and granular casts and occasional red blood corpuscles. Temperature varied from 99°-102° during stay. There was considerable vomiting after admission. Small amounts of nourishment were best administered through the nose. There was some improvement both in the intestinal and eye condition, and the child was discharged at the parents' request, against advice, July 14, improved.

*Diagnosis.*—Mal-nutrition; dyspeptic diarrhœa; ophthalmia with corneal ulcers.

## Discussion.

*Clinical Diagnosis.*—It is at once noticed that these cases are distinctly milder in type than most of those already referred to. Three could most properly be called examples of dyspeptic diarrhœa, and two of indigestion. In one there was marked eczema in addition and in another evidence of prolonged mal-nutrition.

*Condition.*—One was admitted in good, three in fair condition, and the marantic infant was almost in collapse when first seen. There was no marked fever in any of the patients.

*Stools.*—The stools were never more than 12 in 24 hours; were mucoid in character, occasionally contained curds and fecal material, never pus or blood.

Vomiting, though generally present during the illness, was marked in but one case. Albumen and casts were found in the urine of the marantic infant, another had considerable colic.

*Diet.*—Two of the group had been fed on condensed milk and three on cow's milk, two of fair and one of good quality.

Slight rickety deformities were noted in all of the cases.

Two of the patients were under observation less than a week, the other three remained about two weeks.

*Result.*—They varied in age from 3 to 17 months. Three were discharged well and two improved.

*Season.*—Two were admitted in June, the remaining three in July.

### *J. Cases with No Pathogenic Organisms.*

Out of the seventy-four cases, in ten the results of the examination of the stools proved negative, that is, no dysentery or other pathogenic organisms and no other bacteria which agglutinated with the patient's blood, or gave any indication of being the cause of the diarrhœal condition, were found.

It should be mentioned, however, that in some of these cases opportunity was not afforded for repeated examination of the dejecta, and in no one which resulted fatally, was an autopsy permitted.

L. D. Clinical No. 27. Age, eight months. Admitted June 23, 1904. Child had never been ill before. Premature birth; weight four pounds. Fed, after the second month, on modified cow's milk. Had been ailing and fretful a week before admission; suddenly became worse with vomiting. Stools were loose and mucoid, six to eight in twenty-four hours. On examination child was found to be pale, rather sparely nourished, somewhat rachitic. Chest and abdomen were negative. Temperature on admission was 103. Child responded to treatment, temperature fell to normal, stools became fecal, and child was discharged well, July 14. In this case antidysentery serum was employed, apparently with some benefit.

*Diagnosis.*—Dyspeptic diarrhœa.

M. E. Clinical No. 37. Age, six months. Admitted June 25, 1904. One of twins. Never well. Fed variously on oat-meal water and milk. Three days before admission present illness began with vomiting of sour milk, followed by diarrhœa. Stools contained much mucus, no blood. History of several convulsions. Rapid loss in weight. Almost constant pain. Child was found to be exceedingly sparely nourished, markedly rachitic, with distended abdomen. Temperature on admission 104°. There was little response to treatment after the first six or eight hours, then the pulse became irregular and rapid, and the child died July 1.

No autopsy.

*Diagnosis.*—Mal-nutrition; dyspeptic diarrhœa.

H. B. Clinical No. 147. Age, five months. Admitted July 16, 1904. The child always has been well. Fed on condensed milk after three months. Acute illness began three weeks before admission, with vomiting. Stools numerous, watery, with considerable mucous; rapid loss in weight; considerable fever. Child was admitted in collapse. Anterior fontanelle sunken, and tongue covered with thrush. Chest markedly rachitic; ab-

domen distended. Head held in hyper-extension, can be bent forward only with force. Kernig's sign present. Reflexes exaggerated. Pupils failed to respond to light. On lumbar puncture 10 cc. of fluid were removed. No organisms found. No increased pressure. Child's condition continued with little improvement. After several days of slight improvement the child went into a collapse and died July 23.

No autopsy.

*Diagnosis.*—Dyspeptic diarrhœa. Symptoms of meningitis.

E. C. Clinical No. 186. Age, six months. Admitted July 23, 1904. Never ill before. Fed on milk of poor quality with cereal water. Three or four weeks before admission diarrhœa commenced. Stools lumpy, contained mucus, but no blood. Had high fever, considerable colic. Lost continuously in weight. On admission child was sparely nourished, pale, fretful. Stools mucoid, three to six a day; no blood. Child, after a long period of uncertainty, began to improve and stools became fecal in character. Patient was discharged, well, August 24. There was little or no elevation of temperature during observation.

*Diagnosis.*—Dyspeptic diarrhœa; mal-nutrition.

M. S. Clinical No. 183. Age, nine weeks. Admitted July 23, 1904. Child never had been ill before, was very small and somewhat premature. After age of ten days fed on modified scalded milk. One week before admission, was seized with considerable vomiting, followed by moderate diarrhœa. Stools retained their fecal character. No history of blood or mucus. Physical examination, negative. Child responded promptly to modified diet. No elevation of temperature. Discharged well, August 4.

*Diagnosis.*—Intestinal indigestion.

B. S. Clinical No. 191. Age, two months. Admitted July 25, 1904. One of twins; never strong; no acute illness before. Had been fed on condensed milk. Two weeks before had been attacked with vomiting and diarrhœa. Stools were green, mucoid in character, and blood was noticed but once; considerable fever during illness. Child was sparely nourished; small. Anterior fontanelles somewhat sunken. Well-marked stigmata of rickets. Abdomen distended. Child had a long illness, responded slowly to treatment; stools, however, gradually became fecal. There was considerable initial loss of weight followed by a gradual gain. Discharged well, August 30.

*Diagnosis.*—Mal-nutrition; dyspeptic diarrhœa.

J. A. Clinical No. 200. Age, four months. Admitted July 27, 1904. Child was sickly; fed on cow's milk and water with no regard to proper modification, after two months. Mother noticed a perceptible loss in weight for the past month. Ten days before admission stools became free, eight to ten in twenty-four hours, still fecal. Child found to be sparely nourished. Cranio-tabes; tongue coated, thrush. Well-marked rosary.

Abdomen distended. Child was drowsy, looked exceedingly ill. Temperature on admission 100°. Child continued in a drowsy, toxic condition. Hard to arouse. Stools were mucoid and fluid. There was no permanent response to treatment and child died August 1.

No autopsy.

*Diagnosis.*—Mal-nutrition; dyspeptic diarrhœa.

L. H. Clinical No. 239. Age, one year. Admitted August 6, 1904. Child gave history of intestinal trouble one week before admission. Recently had been fed on cold milk. After two weeks of apparently complete recovery, was taken ill with marked vomiting and purging. Stools, twenty in twenty-four hours, green, mucoid, watery, no blood. Considerable fever. Child was found to be sparely nourished; markedly sunken fontanelles. Definitely rachitic. Patient responded slowly to change in diet and treatment. Temperature while at Sanitarium varied from 98°-101°.

Discharged, well, August 18.

*Diagnosis.*—Dyspeptic diarrhœa.

C. B. Clinical No. 251. Age, eight months. Admitted August 9, 1904. Never ill before. Fed on a proprietary food. One month before present illness began with diarrhœa and vomiting. Stools, twenty in twenty-four hours, contained mucus; no history of blood. Considerable tenesmus. Fever reached 104° during illness. Treated for malaria. History of severe fainting attacks before admission. Child was found to be well-nourished, rachitic, markedly toxic; abdomen, negative. Temperature during stay at Sanitarium varied from 98°-104°. The child, however, responded promptly to treatment. Stools never contained blood, and gradually assumed a fecal character. Discharged well, August 18.

*Diagnosis.*—Dyspeptic diarrhœa.

A. S. Clinical No. 249. Age, two years. Admitted August 10, 1904. Never ill before. Table diet. Ten days ago the present illness commenced with diarrhœa. Stools, seven to ten in twenty-four hours, green, mucoid. Considerable fever. Child was found to be poorly nourished, markedly rachitic, unable to walk. Definite Harrison's groove. Stools, for most part, were semi-formed, largely fecal, once blood-tinged. Child did well, and was discharged August 27.

*Diagnosis.*—Dyspeptic diarrhœa.

## Discussion.

*Diagnosis.*—This group includes no instance of definite ileo-colitis. In nine the intestinal infection is of the toxic character, and in one the diagnosis of intestinal indigestion was made. Mal-nutrition of more or less degree was noticed in four cases and in one there were symptoms indicative of meningitis.

*Condition.*—The condition of these babies on admission was only fair in four instances. In five there was evidence of toxemia; one was in collapse.

*Temperature.*—In most of the cases there was marked elevation of temperature, 98°-103° or 104° being noted in several instances. The temperature of the patient thought to have meningitis varied from 94° to 106°.

*Stools.*—The stools, 4 to 20 in number, were semi-fluid and mucoid in character with one exception, the child with intestinal indigestion in whose dejecta fecal material was frequently noted. No macroscopic pus was present and blood was seen only once, and that but a slight fleck.

Vomiting was frequent and in two cases extreme.

Marked abdominal distension was present in two patients, and rectal tenesmus in another.

Thrush was troublesome in two instances.

*Diet.*—Of these ten cases four had been fed on condensed milk, five on cow's milk (two of fair and three of bad quality) and one on table-diet.

The rickety deformities were noted in eight cases. Three of the patients were under observation less than one week, three between one and two weeks, and four longer.

*Age.*—They varied in age from 2 to 24 months, the average being 7.7 months.

Two cases were admitted in June, four in July and four in August.

Of the ten cases eight were discharged well and two died. One of the latter was the suspected meningitis case and the other a marantic infant brought in in collapse.

## Summary.

The results of this investigation conducted in the wards and laboratory of the Sanitarium seem to warrant the following brief statements:

1. The series of cases forming the basis of this study were infants admitted seriatim to The Thomas Wilson Sanitarium suffering from diarrhœa, or those whose stools were found to be frequent after admission. No attempt was made to select cases as especially suitable for examination. In the series are included examples of nearly all the

clinical varieties of intestinal diseases common to young children in the summer, occurring in widely separated sections of the city of Baltimore. In every instance the illness began in the patients' homes, and many of the babies were brought to the Sanitarium late in the course of the disease often in a state of marked mal-nutrition. For this reason the prognosis was of necessity graver than for the average diarrhœal case, when promptly treated.

2. In our bacteriological studies we endeavored to isolate from all the dejecta or at autopsy all dysentery bacilli, streptococci, and organisms agglutinating with the patient's blood found.

Of the 74 cases studied in 42 or 58.3% some variety of the dysentery bacillus was found corresponding to one of the four recognized types either in the stools or in the intestinal tract at necropsy. In these 42 cases no streptococci or organisms other than dysentery bacilli agglutinating with the blood of the patient were isolated. In 11 additional cases, or 14.8% of the whole number, dysentery bacilli were present in association with pathogenic streptococci. In 6 cases, or 8.2%, streptococcus pyogenes was the only pathogenic organism isolated. Streptococci were therefore found altogether in 17 cases, or 22.9% of the series.

Some other micro-organisms which were pathogenic to laboratory animals and which agglutinated with the blood of the patient were isolated alone in each of 4 additional cases. In a fifth case a non-pathogenic bacillus pyocyaneus was the only organism, agglutinating with the patient's blood, which was isolated. In 10 cases no pathogenic organisms were found in the stools. A majority of these cases were admitted late in the season and discharged before more than the examination of a single stool could be completed.

3. The presence of bacilli belonging to the dysentery group in the dejecta of such a large proportion of these cases affected with diarrhœa, and the failure in many of them to find other pathogenic organisms suggests the probability that the dysentery bacillus may be largely responsible for many of these disorders. This view is strengthened by the finding of an almost pure culture of dysentery bacilli in the membrane of a case of extensive diphtheritic ileo-colitis. Our results would [illegible] many [illegible] other organisms, particularly the streptococcus pyogenes, are responsible for certain instances of diarrhœa during the summer months, nor would they controvert the assertion that alterations in the intestinal tract brought about by chemical pro-

cesses or even mechanical means, independent of bacteria, may produce conditions similar to those now under discussion. Stools containing pus, macroscopic or microscopic, were the most favorable for the isolation of the dysentery bacillus.

4. The dysentery bacillus is usually confined to the intestinal tract, although searched for elsewhere in all our autopsies, it was found but twice, once in the liver and once in the mesenteric glands.

5. All of the 172 separate isolations of dysentery bacilli obtained from the 53 positive cases were found to be identical with one of the four recognized types of this organism, as determined by fermentation tests.

6. Organisms, apparently identical to Bacillus "B" (Duval and Schorer) belonging to the group of "dysentery-like" bacilli recently discussed by Torrey, were found in two cases.

7. Agglutination tests with the patient's blood cannot be relied upon to determine infection with *B. dysenteriæ*. The blood of the patient agglutinates the dysentery bacillus isolated from the same case more frequently than it does the stock cultures of the Flexner-Harris group.

Other organisms than the *B. dysenteriæ* found in the stools and organs produced agglutinins in a few cases.

8. Each member of the dysentery group studied agglutinates in highest dilution with its own homologous serum. By absorbing a serum with all but one group the specific agglutinins of that group can be more accurately determined.

An organism belonging to any group will not always absorb the agglutinins of the identical groups in the different immune sera.

9. The Flexner-Harris type of the dysentery organism has the largest amount of agglutinins common to the other members of the dysentery group.

10. Although deductions must be warily drawn from a small number of cases, it would seem that the variety of the dysentery bacillus most frequently associated with the diarrhœal disorders of infants in summer is the type known as Hiss and Russell's "Y," Group II, and that after this in order of frequence comes the Flexner-Harris variety (Group III) and the Shiga type (Group I), respectively.

The comparatively small number of infants infected with the original Shiga strain may partially explain the unsatisfactory results of treatment with serum: for it is only with dysentery of this variety that

a soluble toxin has been produced. The favorable results reported of the serum injection have probably been in cases infected with the original Shiga strain.

Cases in which several types of the organism are present together are common, about equal in number to those associated with the Hiss "Y" type alone. In these "combined" cases the Groups II and III predominate. Group IV (Strong) was present only together with other varieties.

11. Differences in the severity of the illness can be noted in the several groups into which the cases have been divided according to the bacterial findings. Thus the largest proportion of instances of ileo-colitis and the highest mortality in any one group were noted in the series associated with more than one type of the dysentery organism. Here twelve out of the thirteen cases were ileo-colitis and nine died, a mortality of 69 per cent. Next in order of the severity of the affection is the group in which streptococci were found together with dysentery bacilli. Of these cases, eleven in number, seven were ileo-colitis and seven, or 63.6 per cent, died.

Of the fourteen cases associated with but one type of dysentery organism those with Group II or Hiss "Y" bacilli seemed most severe. Six of them were instances of ileo-colitis and seven of them, or 50 per cent, ended fatally.

The cases belonging to Groups I and III, and those in whose stools streptococci alone were found were on the whole less severely ill and presented a considerably lower death rate.

There were no extremely ill patients among those in whose dejecta unclassified dysentery bacilli, or pathogenic micro-organisms other than dysentery bacilli, or streptococci, were present.

12. Of the 74 cases in our series 39 had been fed on condensed milk antecedent to their illness. The remaining 35 had received cow's milk, usually of inferior quality, or table diet.

Of the former number, 12 recovered, 6 were improved, 1 was unimproved, and 20 died, a mortality of 74 per cent. Of those given cow's milk or table diet, 18 recovered, 6 were improved, and 11 died, a mortality of 31 per cent. Our cases, therefore, support the consensus of clinical experience that condensed milk as a food for long periods tends to weaken the infant's constitution and lower its resistance to disease. Although it may be useful as a temporary expedient in infant feeding, especially in hot weather, when a good milk supply and adequate refrigeration are not available.

References.

1. Knox. A Contribution to the Study of the Summer Diarrhœas of Infancy. Jour. of the Am. Med. Assoc., 1903, xli, 173.
   —— A Summer's Experience with Infantile Dysentery. Jour. of the Am. Med. Assoc., 1904, xliii, 1849 and 1924 (Dec. 17).
2. Strong. Bacillus Shiga in an Epidemic of Diarrhœa. Bost. Med. and Surg. Jour., 1903, cxlviii, 331.
3. Pease and Shaw. The Etiology of the Summer Diarrhœas of Children and of Dysentery of Bacterial Origin. Albany Med. Annals, 1904, xxv, 154.
4. Bacteriological and Clinical Studies of the Diarrhœal Diseases of Infancy with Reference to the Bacillus dysenteriæ (Shiga). (See Clinical Studies by Dr. Holt.) Studies from the Rockefeller Inst., 1904, ii, 185.
5. Dunn. Etiology and Classification of the Summer Diarrhœas in Infancy. Arch. of Ped., 1905, xxii, 401.
6. Martini and Lentz. Ueber die Differenzierung der Ruhrbacillen mittels der Agglutination. Zeit. f. Hyg., 1902, xli, 540.
7. Hiss and Russell. Study of a Bacillus Resembling the Bacillus of Shiga. N. Y. Med. News, 1903, Vol. 82, 289.
8. MacConkey and Hill. Bile Salt Broth. II. The Behavior in Bile Salt Broth, in Certain Sugars, and in Glycerine, of some of the Commoner Organisms, etc. Thompson Yates Lab. Reports IV, part I, 1901, 160 (table).
9. Hiss. On Fermentative and Agglutinative Characters of Bacilli of the "Dysentery Group." Jour. of Med. Res., 1905, xiii, 1, 51.
10. Torrey. A Comparative Study of Dysentery and Dysentery-like Organisms. Jour. of Exp. Med., 1905, viii, 365.
11. Duval and Schorer. Bacteriological and Clinical Studies, etc. Rockefeller Inst., 1904, II, 42.
12. Duval. Another Member of the Dysentery Group. Jour. of the Amer. Med. Assoc., 1904, xliii, 381
13. Winne. A report upon the Agglutination Reactions of the Bacillus Dysenteriæ (Shiga) with the Blood Serum of Patients Suffering with Summer Diarrhœa. Johns Hopkins Hosp. Bull., 1905, xvi, 93.
    Also Bacteriological and Clinical Studies, etc. Rockefeller Inst., 1904, I, 118.

14. Eisenberg. Ueber die Verwandschaft der verschiedenen Dysenteriestämme. Wien. klin. Wchnschr., 1904, Vol. 17, 1142.
15. Jehle. Neue Beiträge zur Bakteriologie u. Epidemiologie der Ruhr im Kindesalter. Jahrbuch f. Kinderheilkunde, 1905, Vol. 62, 547.

# AN ANALYTICAL STUDY OF ACUTE LOBAR PNEUMONIA IN THE JOHNS HOPKINS HOSPITAL, FROM MAY 15, 1889, TO MAY 15, 1905.

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During this period of 16 years, 658 patients suffering from acute lobar pneumonia have been treated in the hospital. These include all patients admitted with the disease as well as those developing a terminal pneumonia.

In these statistics the ether pneumonias do not enter. The figures as regards infantile pneumonia, can only be approximately estimated on account of the relatively few cases in a general, as compared to a children's hospital.

Of the total number of patients (658) 200 died, giving us a mortality of 30.39%, from which number if we subtract the 35 terminal pneumonias, we get a mortality of 165, or 25.07%. This compares very favorably with the average hospital mortality, though high when compared with the results of private practice.

*Year.*—The following table and chart show the yearly number of patients with pneumonia and their mortality:

TABLE I.

| Year. | Recovered. | Died. | Total. | Mortality %. |
|---|---|---|---|---|
| May 15, 1889-1890 | 3 | 3 | 6 | 50.0 |
| 1890-1891 | 9 | 2 | 11 | 18.18 |
| 1891-1892 | 11 | 5 | 16 | 31.25 |
| 1892-1893 | 8 | 5 | 13 | 38.46 |
| 1893-1894 | 17 | 11 | 28 | 39.28 |
| 1894-1895 | 23 | 10 | 33 | 30.30 |
| 1895-1896 | 19 | 9 | 28 | 32.14 |
| 1896-1897 | 22 | 12 | 34 | 35.29 |
| 1897-1898 | 28 | 10 | 38 | 26.31 |
| 1898-1899 | 31 | 10 | 41 | 24.39 |
| 1899-1900 | 22 | 14 | 36 | 38.88 |
| 1900-1901 | 50 | 29 | 79 | 36.70 |
| 1901-1902 | 57 | 21 | 78 | 26.92 |
| 1902-1903 | 42 | 14 | 56 | 25.00 |
| 1903-1904 | 36 | 11 | 47 | 23.40 |
| 1904-1905 | 47 | 22 | 69 | 31.86 |
| 1905-May 15 | 33 | 12 | 45 | 26.66 |
| Total | 458 | 200 | 658 | |

As regards merely the frequency of pneumonia, judging from the figures before us, there was a steady increase in the number of patients admitted up to 1899; this may be well accounted for by the growth of the hospital. The marked increase, however, in 1900 and 1901 seems

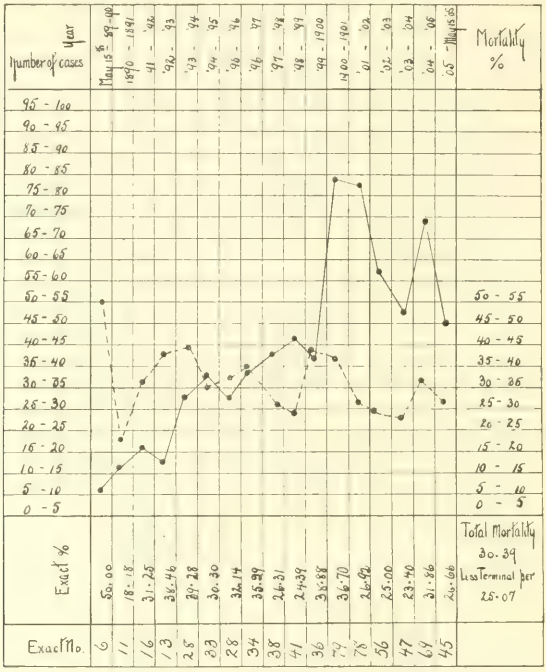


CHART 1.

Continuous line shows number of cases.
Broken line shows mortality percentage.

to indicate an increase in the prevalence of the disease itself during these years, which is partly accentuated by the decreased number of patients during the next two years. Since then, during 1904 there has been another rise in the number admitted, and although the first

five months of 1905 show a relative decrease, yet our total admissions for the year (1905) have gone above those of 1904 and reached 71 patients. (These last figures cannot enter into our statistics, which ended on May 15, 1905.)

In considering the mortality along with these figures and disregarding 1889 on account of the few patients, we note a high percentage of deaths in 1892, 1893, 1896, 1899, and 1900 with a slight rise again through 1904. (In considering the total mortality for the year 1905 and not the first five months, we find a continued rise.)

Comparing these figures with the mortality figures from the State Board of Health of Maryland, 1900 shows a definite increase in mortality, agreeing with our figures for that year. From a comparison of other years no conclusions can be drawn.

*Age.*—The greater frequency of pneumonia in young adults is well brought out in our figures: between 20 and 40 years about 55% of our cases occurred; between 20 and 30 years about 32%; and between 20 and 25 years 18%.

The following age table and chart show the number of patients for each five years of life, and the mortality percentage:

TABLE II.

| Age. | Recovered. | Died. | Total. | Mortality %. |
|---|---|---|---|---|
| Under 1 Year | 2 | 1 | 3 | 33.33 |
| 1- 5 | 20 | 2 | 22 | 9.99 |
| 5-10 | 24 | 1 | 25 | 4.0 |
| 10-15 | 11 | 2 | 13 | 15.3 |
| 15-20 | 46 | 10 | 56 | 17.8 |
| 20-25 | 98 | 20 | 118 | 16.9 |
| 25-30 | 73 | 21 | 94 | 22.3 |
| 30-35 | 61 | 19 | 80 | 23.7 |
| 35-40 | 44 | 26 | 70 | 37.1 |
| 40-45 | 25 | 20 | 45 | 44.44 |
| 45-50 | 25 | 18 | 43 | 41.8 |
| 50-55 | 13 | 17 | 30 | 56.6 |
| 55-60 | 5 | 7 | 12 | 58.3 |
| 60-65 | 3 | 15 | 18 | 83.3 |
| 65-70 | 2 | 10 | 12 | 83.3 |
| 70-75 | 3 | 6 | 9 | 66.6 |
| 75-80 | 2 | 1 | 3 | 33.33 |
| 80-85 | 0 | 1 | 1 | 100.0 |
| 85-90 | 1 | 0 | 1 | 0.0 |
| Total | 458 | 197 | 655 | |

In Chart 2 we see the very marked increase in the total admissions up to the age of 20-25 years where the maximum is reached, with a steady decrease in number, with advancing years. The mortality curve is most interesting, showing a comparatively high mortality under one

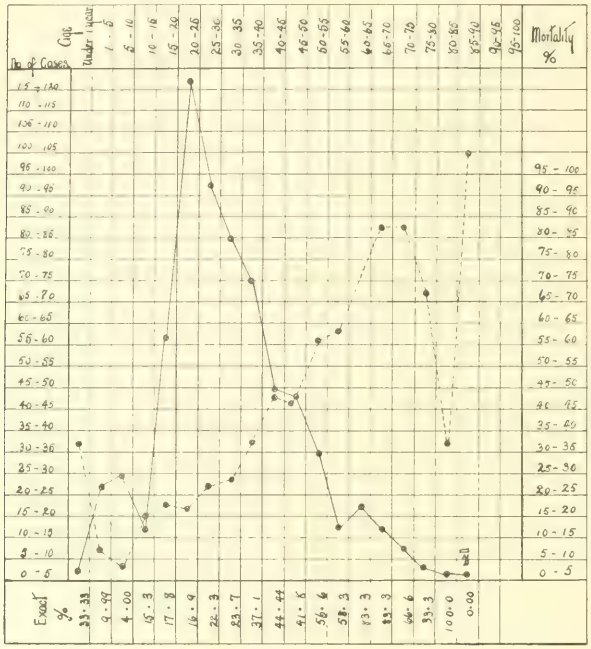


CHART 2.

Continuous line shows number of cases.
Broken line shows mortality percentage.

year, then a steady rise, with a maximum death-rate between 60-70 years or higher. Between 80 and 90 years we had only two patients; one died, the other recovered.

*Sex.*—As we see from the following figures the number of males attacked far outnumber the females, but the mortality among the females is considerably higher, thus:

TABLE III.

| | Recovered. | Died. | Total. | Mortality %. |
|---|---|---|---|---|
| Male ..... | 379 | 154 | 533 | 28.8 |
| Female ..... | 79 | 46 | 125 | 36.8 |

This increased mortality among the females may be explained by their weaker powers of resistance, and by their poorer physical condition on admission.

*Condition.*—Most of the patients were single persons, thus:

TABLE IV.

| | Recovered. | Died. | Total. | Mortality %. |
|---|---|---|---|---|
| Single ..... | 309 | 85 | 394 | 21.5 |
| Married ..... | 120 | 69 | 189 | 36.5 |
| Widowed ..... | 23 | 38 | 61 | 62.2 |

These figures, especially in the percentage of deaths, apparently follow the age curve closely, as the widowed were usually above the average age.

*Race and Nationality.*—In the white population we have the following figures:

TABLE V.

| | Recovered. | Died. | Total. | Mortality %. |
|---|---|---|---|---|
| Male ..... | 130 | 56 | 186 | 30.1 |
| Female ..... | 35 | 17 | 52 | 32.6 |
| | 165 | 73 | 238 | 30.6 |
| Foreign ..... | 120 | 50 | 170 | 29.4 |
| | 285 | 123 | 408 | 30.14 |

In the negro population there were:

| | Recovered. | Died. | Total. | Mortality %. |
|---|---|---|---|---|
| Male ..... | 140 | 58 | 198 | 29.2 |
| Female ..... | 28 | 19 | 47 | 40.4 |
| | 168 | 77 | 245 | 31.4 |
| West Indies .. | 4 | 1 | 5 | 20.0 |
| | 172 | 78 | 250 | 31.2 |

In considering some of the separate nationalities we obtain the following figures:

TABLE VI.

| | | Recovered. | Died. | Total. | Mortality % |
|---|---|---|---|---|---|
| German | Male | 48 | 18 | 66 | 27.0 |
| | Female | 5 | 3 | 8 | 37.0 |
| Irish | Male | 18 | 8 | 26 | 30.0 |
| | Female | 1 | 2 | 3 | 66.0 |
| Russian Jew | Male | 7 | 2 | 9 | 22.0 |
| | Female | 2 | 1 | 3 | 33.0 |
| Pole | Male | 8 | 1 | 9 | |
| | Female | 1 | 1 | 2 | |
| Bohemian | Male | 4 | 1 | 5 | |
| | Female | 1 | 3 | 4 | |
| West Indies | Male | 4 | 1 | 5 | |
| Austrian | Male | 3 | 1 | 4 | |
| Scotch | Male | 1 | 3 | 4 | |
| Norwegian | Male | 3 | 1 | 4 | |
| Canadian | Female | 3 | 1 | 4 | |
| Lithuanian | Male | 2 | 0 | 2 | |
| | Female | 1 | 0 | 1 | |
| Italian | Male | 2 | 1 | 3 | |
| English | Male | 1 | 1 | 2 | |
| Dane | Male | 2 | 0 | 2 | |
| Hungarian | Male | 1 | 0 | 1 | |
| Holland | Female | 1 | 0 | 1 | |
| Welsh | Male | 1 | 0 | 1 | |
| Greek | Female | 1 | 0 | 1 | |
| Syrian | Male | 1 | 0 | 1 | |
| Roumanian | " | 1 | 0 | 1 | |
| Portugese | " | 0 | 1 | 1 | |
| Russian | " | 1 | 0 | 1 | |
| Swede | " | 1 | 0 | 1 | |

Among the points to be noted here are that the foreign born population shows a slightly lower mortality than the native white, being almost the same as the male negro percentage; also that due to the high mortality among the negro female population, the total negro mortality rises somewhat above the total white mortality.

*Months.*—The seasonal and monthly variation in the number of patients and mortality is interesting, as in

TABLE VII.

| Months. | Recovered. | Died. | Total. | Mortality %. |
|---|---|---|---|---|
| January ..... | 58 | 30 | 88 | 34.09 |
| February ..... | 62 | 24 | 86 | 27.4 |
| March ..... | 83 | 33 | 116 | 28.4 |
| April ..... | 61 | 24 | 85 | 28.2 |
| May ..... | 40 | 13 | 53 | 24.5 |
| June ..... | 16 | 10 | 26 | 38.4 |
| July ..... | 9 | 10 | 19 | 52.6 |
| August ..... | 18 | 6 | 24 | 25.0 |
| September ..... | 13 | 11 | 24 | 45.8 |
| October ..... | 19 | 13 | 32 | 40.6 |
| November ..... | 41 | 9 | 50 | 18.0 |
| December ..... | 38 | 17 | 55 | 30.9 |

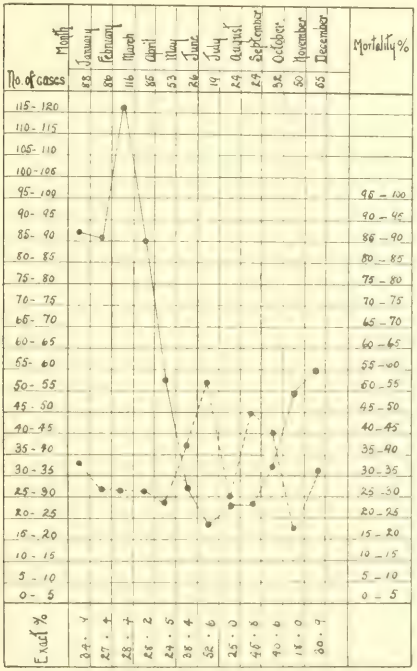


CHART 3.

In looking over Chart 3 we are struck at once with the greater number of patients in March from which the number steadily and quickly diminishes through the late spring and summer months, to begin a steady rise through the fall and winter months.

Comparing with this the mortality curve we note the steady average number of deaths through the winter and fall months, but in the late spring, summer and early fall, the mortality shows more variation and is higher.

Owing to the apparent low mortality in August and the number of our cases being small it is unwise to draw any definite conclusions as regards increased summer mortality.

*Occupation.*—As usual the most frequent occurrence of pneumonia with a higher mortality is to be seen in the outdoor occupations, thus:

TABLE VIII.

| | Recovered. | Died. | Total. | Mortality %. |
|---|---|---|---|---|
| Outdoor | 229 | 118 | 347 | 34.0 |
| Indoor | 201 | 73 | 274 | 26.6 |

The nature of the occupation was as follows:

| Name. | Recovered. | Died. | Total. | Mortality %. |
|---|---|---|---|---|
| Laborers | 130 | 73 | 203 | 35.9 |
| Housework | 26 | 18 | 44 | 40.9 |
| Stevedore | 15 | 8 | 23 | 34.7 |
| Sailor | 21 | 5 | 26 | 19.2 |
| Driver | 14 | 7 | 21 | 33.3 |
| Farmer | 14 | 6 | 20 | 30.0 |
| Scholars | 18 | 2 | 20 | 10.0 |
| Laundress | 8 | 5 | 13 | 38.4 |
| Cook | 8 | 5 | 13 | 38.4 |
| Tailor | 10 | 3 | 13 | 23.0 |
| Clerk | 8 | 3 | 11 | 27.0 |
| Oyster shucker | 9 | 1 | 10 | 10.0 |

The remaining 184 cases were distributed among 66 other occupations, each being represented by from one to eight cases; but it does not seem worth while to tabulate these, and to calculate their percentage mortality, as the resulting figures are so small as to be valueless.

From the figures given we note, as in most hospital statistics, the preponderance of the laboring classes with a mortality from 30-35%. In the female occupations, especially cooking and laundry work, there is a very high mortality, about 38-40%.

*Smoking.*—The question of the use of tobacco was not always determined, yet of the 44 patients that denied the use of tobacco 15 (34%) died. Of these that used tobacco, 235 in all, 118 were moderate users, 39 (33%) of whom died; 117 were heavy smokers: 27 (23%) died.

The total percentage of the general users of tobacco was 35.7% with a general mortality of 28%.

*Alcohol.*—There was a history of the use of alcohol in 426 (64.7%) patients, with a total mortality of 30.9%. The use of alcohol was denied by 62 patients, 15 (24.2%) of whom died. Of the 216 moderate users, 66 (30.5%) died; 144 were heavy drinkers with 47 (32.6%) deaths. Of steady users of alcohol 19 died out of 66 (28.7%) patients. There were 30 who gave a history of sprees before admission; of these 8 (26.6%) died.

As regards mortality, tobacco had little if any influence; but the mortality in users of alcohol was over our general average.[1]

*Previous Diseases.*—The number of previous attacks of pneumonia that a patient may have had is a point of much interest: 88 patients had one attack; 8, two attacks; 3, three attacks, and 1, four attacks of pneumonia.

Rheumatism occurred once in each of 52 patients; one had two attacks, and another three attacks previously.

Thirty-seven patients had had typhoid; 4, tuberculosis; 2, empyema, and 2 diabetes.

*Condition before Admission.*—121 (19.9%) had been exposed to bad weather, and 8 to extremes of temperature. There were 8 cases in nurses and hospital orderlies; 1 orderly was in attendance on patients with pneumonia, but in the histories of the other nurses and orderlies, and of the 3 doctors, no note is found as to their contact with patients with this disease. The past health had been good in 325, and bad in 149 patients.

*Family History.*—There was a family history of tuberculosis in 75 (11.3%) patients. (All tuberculous pneumonias have been excluded from our series.) Pneumonia occurred in the family history in 21 (3.1%) patients.

[1] To get an approximate estimate of the frequency of pneumonia in users of tobacco and alcohol we would have to include those cases in which the previous history as regards habits was not obtainable or asked about. If so we get the following: Tobacco, 35.7 per cent; alcohol, 64.7 per cent, which figures can only be partially correct.

*Symptomatology* (symptoms which patient noticed when first taken ill).[2]

TABLE IX.[3]

| Occurrence of symptoms at onset. | Times. | Per cent. |
|---|---|---|
| Pain in chest | 270 | 41.0 |
| Chills | 234 | 34.0 |
| Cough | 232 | 33.9 |
| Headache | 130 | 19.7 |
| Fever | 127 | 19.3 |
| Weakness | 106 | 16.0 |
| Dyspnœa | 67 | 10.1 |
| Vomiting | 54 | |
| Pain in abdomen | 37 | |
| Chilliness | 35 | |
| Sweats | 32 | |
| Bloody sputum | 29 | |
| Sputum | 22 | |
| General pains | 23 | |
| Pain in the back | 20 | |
| Nausea | 18 | |
| During typhoid | 18 | |
| Anorexia | 14 | |
| Epistaxis | 11 | |
| With a cold | 10 | |
| Sore throat | 6 | |
| Traumatic | 5 | |
| Pain in lower back | 5 | |
| Drowsiness | 5 | |
| Rheumatic pains | 4 | |
| Dizziness | 4 | |
| Diarrhœa | 4 | |
| Pain in shoulder | 3 | |
| Cardiac pain | 3 | |
| Nephritic | 3 | |
| Convulsions | 2 | |
| Fainting | 2 | |
| Aneurismal | 2 | |
| Unconsciousness | 2 | |
| Pain below ribs | 1 | |
| Hiccoughing | 1 | |

[2] In some instances (as in the terminal pneumonias), however, the symptoms of the previous disease are noted.

[3] In Tables IX, X, XI, the percentages below 10 per cent have not been worked out, as they are unimportant.

TABLE IX—Continued.

| Occurrence of symptoms at onset. | Times. |
|---|---|
| Tuberculous | 1 |
| Hæmoptysis | 1 |
| Insidious | 1 |
| After opium poisoning | 1 |
| Cerebral tumor | 1 |
| Constipation | 1 |
| Earache | 1 |
| Pain in eyes | 1 |

In this list the classical onset-symptoms of pneumonia stand out very prominently as indicated by pain, chills, cough and headache.

*Complaints of Patient* (symptoms which he mentioned when his history was taken, after admission to the hospital).

TABLE X.

| Complaint. | Times. | Per cent. |
|---|---|---|
| Cough | 215 | 32.6 |
| Pain in right side | 215 | 32.6 } 56.4 |
| Pain in left side | 157 | 23.8 } |
| Dyspnœa | 109 | 16.5 |
| Headache | 84 | 12.7 |
| Fever | 91 | 13.8 |
| Weakness | 49 | |
| Chills | 42 | |
| Pain in abdomen | 40 | |
| Pain in back | 38 | |
| General pains | 30 | |
| Pneumonia | 29 | |
| Heavy cold | 22 | |
| Delirium | 12 | |
| Typhoid fever | 11 | |
| Bloody sputum | 10 | |
| Sore throat | 9 | |
| Anorexia | 8 | |
| Pain in limbs | 7 | |
| Cardiac pain | 6 | |
| Convulsions | 5 | |
| Dizziness | 5 | |
| Heart disease | 4 | |
| Pains in neck | 4 | |
| Rheumatism | 4 | |
| Pain in lumbar region | 2 | |

TABLE X—Continued.

| Complaint. | Times. |
|---|---|
| Pain below ribs | 2 |
| Diabetes | 2 |
| Grippe | 2 |
| Diarrhœa | 2 |
| Vomiting | 2 |
| Earache | 2 |
| Biliousness | 2 |

Here again pain, cough, and dyspnœa stand out prominently.

The following complaints were each recorded once: Epistaxis, stiffness, muscular twitching, dysentery, malaria, dry mouth, cold in lungs, traumatism, asthma, hiccoughing, jaundice, hoarseness, dry throat, chilliness, trouble with right lung, spitting bile, thirst, nausea, typhoid pneumonia, nephritis and pleurisy.

*Symptomatology* (symptoms noted during patient's illness or stay in hospital)—General pain in chest was by far the most frequent and constant symptom, occurring 525 (79.7%) times.

TABLE XI.

| Symptoms. | Times. | Per cent. |
|---|---|---|
| Dyspnœa | 447 | 66.4 |
| Fever | 346 | 52.5 |
| Chills | 325 | 49.3 |
| Headache | 320 | 48.63 |
| Pain in right side | 307 | 46.6 |
| Weakness | 266 | 40.4 |
| Bloody sputum | 196 | 29.7 |
| Pain in left side | 194 | 29.4 |
| Vomiting | 177 | 26.9 |
| Sputum | 102 | 15.5 |
| General pains | 68 | 10.3 |
| Sweating | 58 | |
| Pain in abdomen | 51 | |
| Nausea | 44 | |
| Epistaxis | 37 | |
| Chilliness | 33 | |
| Anorexia | 25 | |
| Pain in back | 22 | |
| Typhoidal symptoms | 13 | |
| Dizziness | 9 | |
| Diarrhœa | 9 | |
| Meningeal | 7 | |
| Sore throat | 7 | |

TABLE XI—Continued.

| Symptoms. | Times. |
|---|---|
| Convulsions | 7 |
| Pain in limbs | 4 |
| Earache | 4 |
| Suffocating feeling | 3 |
| Mental features | 3 |
| Cardiac pain | 3 |

Occurring twice each were: pain below ribs, pain in neck, stiffness, constipation, stiff neck, abdominal distension, rheumatism, haemoptysis, hiccough, pain in eyes, and once each collapse, unconsciousness, pain in jaw, and ærophagia.

*Pulse.*—The rate of the pulse has been divided into *slow* when below 90 to the minute, of which there were 22 (3.3%) instances, of these 3 (13.6%) died; *medium* when between 90-125, being thus in 334 (50.7%) patients; of these 50 (14.9%) died. Above 125 it was considered as *rapid*, and was found so in 289 (43.9%) patients; of these 143 (49.4%) died.

*Character.*—The character of the artery and pulse was as follows:

TABLE XII.

| Character. | Total Times. | Fatal. | Mortality %. |
|---|---|---|---|
| Good volume and tension | 224 | 19 | 8.4 |
| Poor " " " | 111 | 59 | 53.1 |
| Fair " " " | 215 | 68 | 31.6 |
| Small " " " | 99 | 36 | 36.3 |
| Irregular in | 97 | 64 | 65.9 |
| Dicrotic | 56 | 16 | 28.5 |
| Sclerotic walls | 36 | 12 | 33.3 |
| Bounding | 16 | 3 | 18.7 |
| Collapsing | 16 | 7 | 43.7 |
| Small and thready | 8 | 4 | 50.0 |
| Paradoxus | 1 | 1 | 100.0 |
| Capillary | 1 | 1 | 100.0 |

*Cough.*—Cough was present and of moderate severity in 481 patients, 141 fatal; severe in 91, 24 fatal; dry in 12, 5 fatal; painful in 15, 4 fatal; paroxysmal in 11, 4 fatal; loose in 8, 3 fatal; racking in 3, 1 fatal. There was no cough in 15 patients.

*Temperature* (see special article)—The maximum point reached by the fever during the course of the pneumonia has been divided as follows:

TABLE XIII.

| Temperature. | Total patients. | Fatal. | Mortality %. |
|---|---|---|---|
| Subnormal below 98.5° F. in | 5 | 2 | 40.0 |
| 98.5° to 102° " " | 39 | 13 | 33.3 |
| 102° " 104° " " | 181 | 49 | 27.07 |
| 104° " 106° " " | 384 | 106 | 27.6 |
| Above....106° " " | 49 | 27 | 55.1 |

The temperature on admission was as follows:

| Temperature. | Total patients. | Fatal. | Mortality %. |
|---|---|---|---|
| Subnormal below 98.5° F. in | 37 | 20 | 43.0 |
| 98.5° to 100° " " | 64 | 28 | 43.0 |
| 100° " 101° " " | 70 | 27 | 39.0 |
| 101° " 102° " " | 93 | 25 | 26.0 |
| 102° " 103° " " | 148 | 29 | 19.0 |
| 103° " 104° " " | 116 | 31 | 26.0 |
| 104° " 105° " " | 104 | 28 | 26.0 |
| 105° " 106° " " | 23 | 5 | 21.0 |
| 106° or above | 3 | 3 | 100.0 |

From these figures we note that the maximum temperature in the greatest number of patients is between 104°-106° F.; and the admission temperature is most often between 102°-104° F.; about one-sixth of the patients entering with a temperature below 100° F.

*Respiration.*—The respiratory rate was below 30 to the minute in 48 patients, 4 (8.3%) fatal; between 30-40 in 208 patients, 31 (14.9%) fatal; between 40-50 in 192, 56 (29.1%) fatal; and over 50 to the minute in 195 patients, 107 (54.8%) fatal.

TABLE XIV.

| Quality. | Total patients. | Fatal. | Mortality %. |
|---|---|---|---|
| Dyspnœa | 367 | 140 | 38.1 |
| Respiration labored | 165 | 71 | 43.0 |
| Cyanosis (slight) | 134 | 58 | 43.2 |
| Cyanosis (marked) | 81 | 35 | 43.2 |
| Expiratory grunt | 65 | 23 | 35.0 |
| Shallow respiration | 35 | 20 | 57.0 |
| Dilation of alæ nasi | 30 | 12 | 40.0 |
| Cheyne-Stokes respiration | 6 | 5 | 83.0 |
| Orthopnœa | 5 | 5 | 100.0 |
| Periods of apnœa | 1 | 1 | 100.0 |
| Respiration not labored | 215 | 17 | .07+ |

*Sputum.*—Its character varied much, as is seen in the following table:

TABLE XV.

| Quality. | Total times. | Fatal. |
|---|---|---|
| Tenacious | 299 | 72 |
| Rusty | 183 | 48 |
| Blood-stained | 169 | 31 |
| Muco-purulent | 144 | 29 |
| Scanty | 92 | 16 |
| Bloody | 83 | 18 |
| Mucoid | 68 | 8 |
| Frothy | 48 | 14 |
| Yellow | 35 | 8 |
| Greenish | 33 | 8 |
| Abundant | 28 | 6 |
| Prune juice | 25 | 11 |
| Pneumonic | 23 | 3 |
| Bile-stained | 15 | 3 |
| Gelatinous | 18 | 3 |
| Purulent | 10 | 2 |
| Layered | 5 | 1 |
| Foul | 5 | 1 |
| No sputum | 36 | 9 |
| Elastic tissue was present | 3 | |

*B. pneumoniæ* were found in the sputum in 93 patients, 23 of which were fatal. Tubercle bacilli were found in 4 patients, all of whom had definite tuberculosis as well as acute lobar pneumonia (tuberculous pneumonias have been excluded from these statistics). No tubercle bacilli were found in 247 other patients in whom the sputum was examined. *B. pneumoniæ* were undoubtedly present in the sputum in a great many more patients, but no positive diagnoses were made unless the diplococci found showed a capsule when specially stained.

*Involvement of the Lungs.*—The right side of the lungs was involved as follows:

TABLE XVI.

| Lobes. | Recovered. | Died. | Total. | Mortality. |
|---|---|---|---|---|
| Upper | 47 | 14 | 61 | 22.9 |
| Middle | 3 | 0 | 3 | 0.0 |
| Lower | 118 | 21 | 139 | 15.1 |
| Apical | 2 | 0 | 2 | 0.0 |
| Upper and middle | 16 | 17 | 33 | 51.5 |
| Upper and lower | 26 | 11 | 37 | 29.0 |
| Lower and middle | 27 | 8 | 35 | 22.9 |
| All lobes | 22 | 22 | 44 | 50.0 |
| | 261 | 93 | 354 | 26.5 |

In considering these figures we note that the right side alone is involved in more than half the patients, with a mortality below the average. The right lower lobe is most commonly involved, with the lowest mortality; the involvement of the upper and middle lobes show the highest mortality.

On the left side the lobes varied as follows:

TABLE XVII.

| Lobes. | Recovered | Died. | Total. | Mortality %. |
|---|---|---|---|---|
| Upper | 13 | 2 | 15 | 13.3 |
| Lower | 91 | 16 | 107 | 14.9 |
| Apical | 1 | 0 | 1 | 0.0 |
| Upper and lower | 29 | 16 | 45 | 35.5 |
| | 134 | 34 | 168 | 20.2 |

We again note that the lower lobe is more frequently involved in the left lung with a fairly low mortality, which rises quite high when both the upper and lower lobes are involved. The left lung is involved in about one-quarter of all the patients, with the lowest mortality when compared with the right side, or involvement of both sides.

In cases of pneumonia of both lungs, we find a mortality of about 54.07%; such cases occurred in about one-fifth (20.5%) of our patients.

The lobar involvement was as follows:

TABLE XVIII.

| | Recovered. | Died. | Total. | Mortality %. |
|---|---|---|---|---|
| Right and left lower | 35 | 23 | 58 | 39.6 |
| " upper and lower; left upper and lower | 6 | 8 | 14 | 57.1 |
| " lower; left upper and lower | 6 | 6 | 12 | 50.0 |
| " side all lobes; left lower | 3 | 9 | 12 | 75.0 |
| " lower and middle; left lower | 3 | 6 | 9 | 66.6 |
| " upper and lower; left lower | 3 | 4 | 7 | 57.1 |
| " upper and left lower | 1 | 4 | 5 | 80.0 |
| " lower; left upper | 1 | 2 | 3 | 66.6 |
| " side all lobes; left upper | 1 | 2 | 3 | 66.6 |
| " upper and middle; left upper and lower | 0 | 2 | 2 | 100.0 |
| " middle; left lower | 1 | 1 | 2 | 50.0 |

The following occurred once each and ended fatally: right lower and middle, and left upper; right upper and lower, and left upper; right middle, and left upper and lower; right upper and middle, left upper;

right upper, left upper and lower; right lower and middle, left upper and lower. The two recovering were right apex and lower, left lower; and right upper and middle, left lower lobe.

The most frequent combination of lobes in double pneumonias was that of the right and left lower, occurring in 8.8%, with a mortality of 39.6%.

*Bacteriology.—B. pneumoniæ* was obtained from the blood during life in 23 out of a total of 91 patients, or about 25.2%. Of these 23 patients, 16 died, or 69.1%. Of the 68 patients from whose blood there was no growth of *B. pneumoniæ,* 56 recovered and 12 died. (See special article.)

Lumbar puncture was done 9 times, in 6 of which the *B. pneumoniæ* were found; 2 gave negative results, but 1 showed the *B. pneumoniæ* in cover-slip smears.

Joints were aspirated in 3 patients (all fatal). Two gave negative results in cultures, and 1 showed the pneumococcus. (See special article).

The Widal reaction was tried in 98 patients, 20 of which gave a positive reaction; all either had typhoid, or had had it previously.

*Leucocytes* (see special article).—A leucocyte count was made in 582 patients, and varied as follows.

TABLE XIX.

| Leucocytes. | Recovered. | Died. | Total. | Mortality %. |
|---|---|---|---|---|
| 0- 5,000 | 2 | 3 | 5 | 60.0 |
| 5,000- 10,000 | 15 | 19 | 34 | 55.8 |
| 10,000- 15,000 | 49 | 24 | 73 | 32.8 |
| 15,000- 20,000 | 66 | 22 | 88 | 25.0 |
| 20,000- 25,000 | 80 | 18 | 98 | 19.3 |
| 25,000- 30,000 | 81 | 19 | 100 | 19.0 |
| 30,000- 35,000 | 46 | 18 | 64 | 28.1 |
| 35,000- 40,000 | 26 | 13 | 39 | 33.3 |
| 40,000- 45,000 | 14 | 6 | 20 | 30.0 |
| 45,000- 50,000 | 16 | 7 | 23 | 30.4 |
| 50,000- 55,000 | 9 | 7 | 16 | 43.7 |
| 55,000- 60,000 | 5 | 2 | 7 | 28.5 |
| 60,000- 65,000 | 5 | 2 | 7 | 28.5 |
| 65,000- 70,000 | 1 | 1 | 2 | 50.0 |
| 70,000- 75,000 | 0 | 2 | 2 | 100.0 |
| 75,000- 80,000 | 1 | 1 | 2 | 50.0 |
| 80,000- 95,000 | 0 | 0 | 0 | 0.0 |
| 95,000-100,000 | 1 | 0 | 1 | 0.0 |
| 100,000-150,000 | 1 | 0 | 1 | 0.0 |

We note in Chart 4 the high mortality where the leucocytosis is small; the mortality steadily decreases with an increase in the number of leucocytes and reaches a minimum at from 20-30,000. The mortality is fairly constant when the leucocytes range from 30-60,000, but there is a marked rise in the death-rate when the leucocytes mount higher;

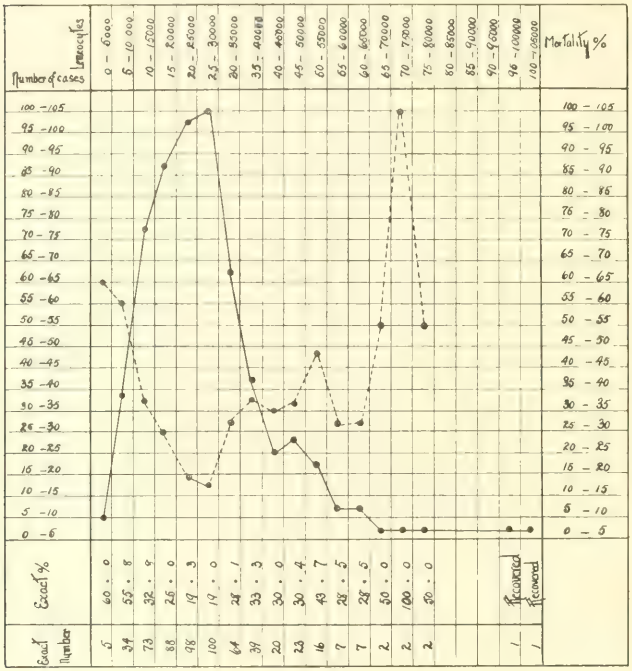


CHART 4.

Continuous line shows number of cases.
Broken line shows mortality percentage.

however, in both of our patients with extreme leucocytosis (one of 95,000, the other of 105,000) recovery took place.

*Urine.*—Albumin was present in 511 (77.6%) patients. There was none in 111 (16.8%) patients. There was a *faint* trace in 83

(16.2%) patients; a *trace* in 352 (68.8%) patients; and a *heavy trace* in 76 (15%) patients. Casts were present in 166 (25.2%) patients.

The diazo reaction was present in 65 (16.8%) patients, and absent in 321 (83.2%) examinations.

Bile was found in the urine of 45 (34.3%) patients, out of 131 examined for it; it was absent in 86 (65.7%).

*Chlorides.*—They were estimated in 103 patients. In 52 (50.4%) examinations of the urine, there was less than 1 gram per litre; in 32 (31%) less than 2 grams; in 13 (12.6%) less than 5 grams; in 4 (3.8%) less than 10 grams per litre, and in 2 (1.9%) less than 15

## Complications.

*Pleurisy* as is usual in pneumonia occurred very frequently (see Table XX). It was found in 338 (51.2%) patients. These figures are undoubtedly low, for a pleuritic rub may be overlooked, or have disappeared when the patient is admitted.

Table XX.

| Pleurisy dry. | Recovered. | Died. | Total. | Mortality %. |
|---|---|---|---|---|
| Right side ..... | 108 | 82 | 190 | 43.1 |
| Left side ..... | 85 | 63 | 148 | 42.5 |
| Pleurisy with effusion. | | | | |
| Right side ..... | 4 | 3 | 7 | 42.8 |
| Left side ..... | 3 | 1 | 4 | 25.0 |

Table XXI.

| Empyema. | Recovered. | Died. | Total. | Mortality %. |
|---|---|---|---|---|
| Right side ..... | 11 | 3 | 14 | 21.4 |
| Left side ..... | 10 | 3 | 13 | 23.0 |

*Empyema* necessitated operation in 22 of the patients, 2 (9.9%) of whom died. (See special article.)

*Pericarditis* was present in 35 patients (5.3%), with a mortality of 31 (88.5%). (See special article.)

*Endocarditis* was found in 13 (1.9%) patients. Ten (76.9%) of these died. (See special article.)

*Jaundice* was present in 76 (11.5%) patients, with 21 (27.6%) deaths. This complication varied somewhat during the different years; thus, it occurred in 1901, 20 times; in 1902, 13 times; in 1903, 9 times; and in 1900 only 6 times, yet this year had the greatest number of pneumonia patients.

*Meningitis* was a very serious complication. It occurred in 13 patients; all of them died. (See special article.)

*Otitis media* was present on one side in 8 patients; 1 patient had a double otitis; all recovered.

*Abscess of the Lung.*—A single abscess was found in 5 patients, one of whom died. Multiple abscesses of the lung occurred 4 times; all these cases were fatal.

*Parotitis* was present in 4 patients; all recovered.

*Conjunctivitis* was present 4 times; with death in one case.

*Thrombosis* (see special article) occurred 3 times; twice in the right popliteal vein, and once in the right internal saphenous vein. One of the patients died.

*Arthritis* occurred 3 times, and in 2 instances the patient died. (See special article.)

| | | | |
|---|---|---|---|
| Peritonitis occurred | 3 | times, | all fatal. |
| Tonsillitis " | 3 | " | all recovered. |
| Pneumothorax occurred | 2 | " | 1 fatal. |
| Gangrene of the lung occurred | 2 | " | 1 fatal. |

The following occurred once each: impairment of speech (recovered); acute nephritis (died); subtrapezious abscess (recovered); keratitis (died), and mastitis (died).

There were 8 patients with "pneumococcus septicæmia"; all died.

*Delirium* occurred in 149 (22.4%) patients; of these 67 (44.9%) died. Twelve patients were admitted in delirium, and of these 7 (58.3%) died.

*Herpes* (see Table XXII) was present in 180 (45.8%) patients and absent in 213. In 265 no note of its presence or absence was made.

TABLE XXII.

| | | |
|---|---|---|
| Lips, both | 28 | |
| Lower | 29 | |
| Upper | 21 | |
| Left angle of mouth | 4 | Lips 87 (48.3%) times. |
| Right angle of mouth | 5 | |
| Total | 87 | |
| Nose | 31 | |
| Right ala nasi | 5 | |
| Left ala nasi | 7 | Nose 43 (23.3%) times. |
| | 43 | |

It was present on the ears in 3 patients; on the right ear twice, and the left ear once; on the left cheek twice; and once each on right buttock and loin; it was submental once; and once respectively on left and right chin. It broke out somewhere on the body of 41 patients, but no note of its site is found in the histories.

*Special Features.*—Delayed resolution 35 (5.3%) times (see special article); a pleuro-pericardial rub 14 (2.1%) times; traumatic pneumonia 5 (0.7%) times; unresolved pneumonia 4 (0.6%) times; central pneumonia 2 (0.3%) times; and relapse 5 (0.7%) times. Several patients were admitted to the surgical division of the hospital, at the onset of the pneumonia for severe abdominal pain. Aside from delirium 5 patients showed mental features, one of whom had an undoubted post-febrile psychosis. There was one instance of an embolic pneumonia following typhoid fever. One patient showed a marked post-critical collapse, and one a marked pre-critical rise in temperature. There was another who showed a peculiar irregularity of the pulse. In one there was the possibility of the lung involvement being a luetic process. One of the typhoid patients in whom a pneumonia developed suffered also from an arterial thrombosis (most probably typhoidal). Terminal pneumonia occurred 35 (5.3%) times (see special article).

*Blood Pressure*[4] varied between 125 and 150 mm. Hg.; in the majority of the 118 patients on whom estimations were made.

TABLE XXIII.

| mm. Hg. | Times. | Per cent. |
|---|---|---|
| 200-175 | 10 | 8.4 |
| 175-150 | 26 | 22.0 |
| 150-125 | 47 | 39.8 |
| 125-100 | 25 | 21.1 |
| 100- 75 | 10 | 8.4 |

*Defervescence* (see special article)—For sake of clearness and comparison we have divided the crises into *true* and *protracted*. *True* when the temperature falls to normal or below in less than 12 hours; and *protracted* when it takes from 12 to 24 hours. A drop of less than

[4] Part of these records were obtained by the instruments with the narrow arm-cuff bands, which have been found to be slightly inaccurate, and give higher readings, than the broad-band instruments.

3° F. has not been considered a crisis. Any drop in temperature lasting longer than 24 hours has been considered as a lysis.

| | Times. | Of total cases. per cent. | Of recovered cases. per cent. |
|---|---|---|---|
| True crisis occurred..... | 99 | 15.0 | 21.6 |
| Protracted crisis occurred... | 71 | 10.8 | 15.5 |
| | 170 | 25.8 | 37.1 |
| Lysis occurred ..... | 288 | 43.7 | 62.8 |

Pseudo-crisis was noted when the temperature fell to about 100° F., and returned to its average height in 12 hours or less. There were 17 (2.5%) such instances.

The association of a fall in the number of leucocytes and the temperature, show some interesting results; thus, in 7 instances the leucocytes fell 5,000 during the crisis; in 25, 10,000; in 16, 15,000; and in 8, 20,000; all of these were true crises. In the protracted crises, 9 times the fall was 5,000; 19 times, 10,000; 9 times, 15,000; and 5 times, 20,000.

The day of crisis was as follows:

TABLE XXIV.

| Day. | True crisis. | Protracted crisis |
|---|---|---|
| 1st ..... | 0 | 0 |
| 2d ..... | 0 | 0 |
| 3d ..... | 1 | 0 |
| 4th ..... | 7 | 4 |
| 5th ..... | 15 | 5 |
| 6th ..... | 14 | 8 |
| 7th ..... | 20 | 24 |
| 8th ..... | 14 | 6 |
| 9th ..... | 16 | 10 |
| 10th ..... | 7 | 6 |
| 11th ..... | 3 | 3 |
| 12th ..... | 0 | 3 |
| 13th ..... | 1 | 0 |
| 14th ..... | 1 | 0 |
| 15th ..... | 0 | 2 |
| Total ..... | 99 | 71 |

These figures bear out the common supposition that the drop in temperature occurs more frequently on the 7th and 9th days; also that the crisis is more common on the odd days (1, 3, 5, 7) etc.; as 100 of the 170 crises fell on the odd days.

*Duration.*—In regard to this point, only the time in the hospital has been considered, as often the history of the date of onset was too indefinite, or could not be obtained.

TABLE XXV.

| Day | Recovered. | Died. | Total. | Mortality %. |
|---|---|---|---|---|
| Under 12 hours..... | 0 | 9 | 9 | 100.0 |
| 1 day ..... | 0 | 22 | 22 | 100.0 |
| 2 days ..... | 0 | 25 | 25 | 100.0 |
| 3 " ..... | 0 | 29 | 29 | 100.0 |
| 4 " ..... | 2 | 20 | 22 | 90.9 |
| 5 " ..... | 3 | 15 | 18 | 83.3 |
| 6 " ..... | 4 | 9 | 13 | 69.9 |
| 7 " ..... | 10 | 12 | 22 | 54.5 |
| 8 " ..... | 9 | 6 | 15 | 40.0 |
| 9 " ..... | 12 | 7 | 19 | 36.8 |
| 10 " ..... | 21 | 9 | 30 | 30.3 |
| 11 " ..... | 18 | 3 | 21 | 14.2 |
| 12 " ..... | 26 | 5 | 31 | 16.1 |
| 13 " ..... | 17 | 4 | 21 | 19.0 |
| 14 " ..... | 26 | 2 | 28 | 7.1 |
| 15 " ..... | 21 | 2 | 23 | 8.7 |
| 16 " ..... | 24 | 0 | 24 | 0.0 |
| 17 " ..... | 16 | 1 | 17 | 5.8 |
| 18 " ..... | 23 | 0 | 23 | 0.0 |
| 19 " ..... | 12 | 2 | 14 | 14.2 |
| 20 " ..... | 22 | 1 | 23 | 4.3 |
| 21 " ..... | 14 | 2 | 16 | 12.5 |
| 22 " ..... | 11 | 2 | 13 | 15.3 |
| 23 " ..... | 10 | 0 | 10 | 0.0 |

There were 156 cases that remained in the hospital from 24 to 237 days; for 24, 25, and 26 days there are records of 9 patients each; for 27 and 29 only 3 each; for 28, 10; and for 30, 11; above 30 days the numbers range irregularly with from 1 to 6 patients for the remaining days; and no conclusions of importance can be drawn from these statistics.

The extreme length of time that many of the patients were in the hospital, was, of course, due to the many complications, or associated conditions occurring synchronously. The high mortality during the first days after admission, was, as in most hospitals, due to the moribund and collapsed condition in which so many patients are received in a general hospital. (Some statistics do not take into account

patients not in the hospitals for 24 hours, which in our series numbered 31, thus increasing our total mortality percentage.)

*Treatment* was limited to a few general procedures.

*Stimulants.*—Strychnia, digitaline, and alcohol, etc., were used in the majority of the patients (536 (81.4%) patients).

*Symptomatic.*—Under this head were included morphia, codeia, heroin, inhalations, and various other drugs. These were used in about 460 (69.9%) patients.

HYDROTHERAPY.

| | | | | | | |
|---|---|---|---|---|---|---|
| Ice-bags | were used | 224 | times, | or | 34.0% |
| Ice-sponges | " " | 189 | " | " | 28.6% |
| Tapwater sponges | " " | 98 | " | " | 14.8% |
| Tubs | " " | 21 | " | " | 3.1% |

GENERAL MEASURES.

| | | | | | |
|---|---|---|---|---|---|
| Infusions | were used | 60 | times, | or | 9.1% |
| Salt solution per rectum | " " | 15 | " | " | 2.32% |
| Poultices | " " | 15 | " | " | 2.25% |
| Anti-pneumococcus serum | " " | 5 | " | " | 0.7% |
| Venesection | " " | 5 | " | " | 0.7% |

Simply rest in bed was tried in 26 patients. Of these procedures little if anything may be said, as all are and have been used by various persons, and in various places, and their merits greatly discussed. Venesection was practically only used as a symptomatic measure in relieving cyanosis, or in engorgement. Anti-pneumococcus serum gave few if any good results, in most instances causing only a slight fall in temperature, while quickening the pulse, and rendering the general condition of the patient worse. In summing up the hospital results of all forms of treatment during sixteen years we note that the mortality changed very little with any form of treatment; the average yearly mortality has remained very much the same; any variations agreeing in most instances with the increased or decreased mortality of pneumonia for the year, and city, as shown in the Board of Health reports.

*Associated Diseases.*—There were many associated diseases the most common being typhoid fever, which occurred 21 (3.1%) times, with a mortality of 52.8%; and chronic nephritis 18 (2.7%) times, though doubtless this latter was present much more frequently, as can be seen in a study of the pathological records. (See special article.)

Cardio-vascular lesions occurred frequently; aortic insufficiency 10 times; mitral insufficiency, 7; mitral stenosis, 4; aortic stenosis, 1; myocarditis, 7; chronic endocarditis, 3; chronic pericarditis, 2; adherent pericardium, 1; arterio-sclerosis was noted 7 times, in the diagnosis, though doubtless present more often, but with no attributed symptoms.

Pulmonary tuberculosis was associated with the pneumonia 9 times; acute articular rheumatism, 7; uræmia, 3; erysipelas, 3; delirium tremens, 3. The following diseases occurred twice each: small-pox, diabetes, cystitis, cholelithiasis, arthritis deformans, pregnancy, chronic alcoholism, aneurism, and diphtheria.

Occurring once each were eclampsia, post-partum infection, trichinosis, ulcerative colitis, opium poisoning, gangrenous stomatitis, uterine hæmorrhage, secondary anæmia, exudative erythema, arthritis, pyuria, infected hand, influenza, abscess of foot, convulsions, pancreatic abscess, spondylitis, acute nephritis, abscess of the buttock, necrosis of superior maxilla, cholecystitis, pernicious anæmia, cerebral tumor, epilepsy, chronic bronchitis, acute peritonitis, hæmoptysis, acute tonsillitis, chronic tuberculous pleurisy, tuberculous peritonitis, and alveolar abscess.

## Open-Air Treatment of Lobar Pneumonia.

On account of the widespread interest in the open-air treatment of lobar pneumonia we have thought it might be interesting to note any changes in our pneumonia records during the last year and a half, in which time there has been a routine open-air treatment of all cases.

In this time (from about January, 1908, to May 15, 1909) there have been 87 cases of acute lobar pneumonia treated in the wards of the hospital, in all of which the treatment was practically the same as in our general series with the exception that the patients were kept out of doors on porches, etc., most of the time. Of these 87 patients, 7 died, giving us a mortality of only 10.8% compared to a mortality in the general statistics of 25.7%.

*Age.*—About one-half of the cases of pneumonia occurred between the ages of 15 and 30 years, with a mortality of only 3%. The mortality in the general statistics for the same age period was 18%. The white and colored patients were about equally divided in numbers admitted.

*Months.*—Fifty of these cases occurred in the months of February, March and April, with only 6% mortality. Figures in the general statistics for the same months were 28%. As the weather during these months is rather severe, these figures speak well for the way the patients improved under the treatment.

*Temperature.*—The temperature as a rule ran a lower course than in the general statistics. In 61 of the patients the temperature was fairly moderate, and in only 17 did it go above 105° F. There seems to be no difference in general as regards the extent of the involvement of the lungs, or the increase in the leucocytes, the counts of the latter being about as usual.

*Complications.*—In regard to complications empyema and otitis were more frequent than usual, about 8% and 4.5%, respectively. This may have been a yearly coincidence, as these complications vary so much from year to year, and may not have any relations to the open-air treatment. As regards the other complications they occurred about as usual.

*Effervescence.*—More of the cases terminated with crisis in the outdoor treatment, crises occurring in 33.7% as compared to 25.8% in general statistics.

*Summary.*—As the number of patients (87) is so few, and the period of time covered being only one and a half years, it is unsafe to draw any conclusions as regards the result of open-air treatment, especially as pneumonia varies somewhat from year to year; however, it might be noted that never in any previous year was there such a low mortality, even when taking into account the patients' ages and differences that otherwise might make favorable conditions. In general the patients stood the open-air treatment splendidly, and they seemed to suffer less from dyspnea, cyanosis and delirium, than similar patients treated indoors.

# A PATHOLOGICAL ANALYSIS OF 195 CASES OF LOBAR PNEUMONIA.[1]

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The anatomical diagnosis of lobar pneumonia has been made in 195 of the 2791 autopsies which have been performed in 17 years (May 15, 1889, to September 28, 1906) at the Johns Hopkins Hospital, or in other words, in about 7% of the autopsies.

| Sex. | Per cent. |
|---|---|
| 137 males were affected, or | 75.0 |
| 45 females " " " | 25.0 |

| Color. | Per cent. |
|---|---|
| White, 95 cases | 52.7 |
| Black, 87 " | 47.3 |
| White males, 74 cases | 40.0 |
| Black " 63 " | 34.4 |
| White females, 21 cases | 11.6 |
| Black " 24 " | 13.3 |

| Age. | Per cent. |
|---|---|
| Up to 10 years, 5 cases | 2.7 |
| 10-20 " 9 " | 4.9 |
| 20-30 " 36 " | 19.7 |
| 30-40 " 39 " | 21.4 |
| 40-50 " 29 " | 20.8 |
| 50-60 " 30 " | 16.4 |
| 60-70 " 17 " | 9.3 |
| 70-80 " 7 " | 3.8 |
| 80-90 " 1 " | 0.5 |

The age varied from under 1 year to over 80 years, but the greater proportion, or 78.8%, occurred between 20 and 60 years of age.

[1] For a clinical analysis during this period see An Analytical Study of Acute Lobar Pneumonia in the J. H. Hospital from May 15, 1889, to May 15, 1905, by J. A. Chatard, M. D., Maryland Med. Jour., Vol. XLIX, No. 10 and 11, pp. 400-405 and 433-436. This analysis extends over another year, and during this time 11 new cases were added.

| Lung involvement. | Per cent. |
|---|---|
| The right lung was affected in 85 cases, or | 44.0 |
| " left " " " " 24 " " | 12.4 |
| Both lungs were " " 84 " " | 43.5 |

An analysis by lobes showed that on the right side

| | Per cent. |
|---|---|
| the upper lobe was involved in 83 cases, or | 32.9 |
| " middle " " " " 48 " " | 19.0 |
| " lower " " " " 94 " " | 37.3 |

All the lobes with the exception of a narrow margin (anterior border) were involved in 27 cases, or 10.7%.

| The amount of involvement. | Slight. | Moderate. | Complete. |
|---|---|---|---|
| Upper lobe | 9 cases, or 10.0%; | 17 cases, or 20.0%; | 57 cases, or 68.0% |
| Middle lobe | 6 " " 12.7%; | 10 " " 20.8%; | 32 " " 66.6% |
| Lower lobe | 8 " " 8.5%; | 29 " " 30.8%; | 57 " " 60.6% |

On the left side the upper lobe was involved in 47 cases, or.. 34.0%
" " " " " lower lobe " " " 83 " " .. 60.0%
Both lobes were involved in 8 cases, or..... 5.7%

| The amount of involvement. | Slight. | Moderate. | Complete. |
|---|---|---|---|
| Upper lobe | 15 cases, or 21.9%; | 16 cases, or 34.0%; | 16 cases, or 34.0% |
| Lower lobe | 7 " " 8.0%; | 23 " " 27.7%; | 53 " " 63.8% |

In the cases of double pneumonia the following combination of lobes were effected:

| | Cases. |
|---|---|
| Right upper with left upper | 3 |
| " " " " lower | 7 |
| " " " " " and lower | 2 |
| " " and middle with left upper | 2 |
| " " " " " lower | 1 |
| " " " " " " upper and lower | 2 |
| " " " lower " " " | 1 |
| " " " " " " " and lower | 5 |
| " " " " " " lower | 3 |
| " middle with left upper | 1 |
| " " " " lower | 1 |
| " " " " upper and lower | 1 |
| " " and lower, with left lower | 3 |
| " " " " " " upper and lower | 1 |
| " lower, with left upper | 1 |
| " " " " lower | 18 |
| " " " " upper and lower | 6 |
| All lobes with left upper | 6 |
| " " " " lower | 12 |
| " " of both sides | 7 |

From this list it appears that the most frequent combination was involvement of both lower lobes, 18 cases, or 21.6%. The next most common was the entire involvement of the right side with that of the left lower lobe, 12 cases, or 14.4%. The right upper and left lower lobes were involved in 7 cases, 8.4%, as were also all the lobes in both lungs. All combinations were present in at least 1 case.

| Stage of Hepatization. | Per cent. |
|---|---|
| Red in 52 cases, or | 25.7 |
| Gray " 64 " " | 31.6 |
| Mixed " 88 " " | 43.5 |

In the double pneumonia red hepatization was present on the left in 12 cases and in 6 cases on the right while gray hepatization occurred in just the reverse frequency. Mixed hepatization was present in the other cases.

Condition of the uninvolved lung tissue:

| This was described as— | Per cent. |
|---|---|
| Congested or œdematous in 144 cases, or | 75.3 |
| Normal " 8 " " | 4.1 |
| Dry " 6 " " | 3.1 |
| Crepitant " 13 " " | 6.8 |

The normal lung tissue was found chiefly on the uninvolved side in those cases of one-sided consolidation.

Condition of the pleuræ: there were notes on the pleural condition in 164 cases, or 84.1%. No pleurisy in 9 cases, or 5.4%; 4 of these cases showed ecchymoses beneath the pleural surface. Fibrinous pleurisy in 155 cases, or 94.6%.

| Of these cases the— | Per cent. |
|---|---|
| Exudate was thick in 29 cases, or | 17.6 |
| " " serous " 30 " " | 18.4 |
| " " hæmorrhagic in 6 " " | 3.6 |
| " " purulent " 9 " " | 5.4 |

The condition of the bronchi were noted in 156 cases.

| | Per cent. |
|---|---|
| Normal in 9 cases, or | 5.0 |
| Injected " 136 " " | 87.0 |
| Containing pus " 32 " " | 2.0 |
| Plugged with fibrin " 8 " " | 5.0 |
| Dilated " 5 " " | 3.2 |

The bronchial lymph glands were mentioned in 70 cases; normal, in 2; congested in 68. Of these 38 were noted as pigmented; 5 as firm; 6 as caseous; 4 as calcified, and 1 showed focal necrosis.

The associated lesions complicating the pneumonia may be mentioned under various systems.

*Nervous System:*

| | Cases. |
|---|---|
| Acute meningitis | 8 |
| Pachymeningitis | 2 |
| Congestion of the choroid plexus | 1 |

*Respiratory System:*

Hydrthorax was found in 5 cases.

| | Per cent. |
|---|---|
| Chronic adhesive pleuritis was presented in 111 cases, or | 56.9 |
| Occurring in 23 cases on the left side, or | 20.7 |
| " " 27 " " " right " " | 24.3 |
| " " 61 " " both sides, " | 54.9 |

Bronchopneumonia was recorded in 18 cases, or 9.2%; interstitial-pneumonia in 5 only.

*Pulmonary:*

| | Cases. | |
|---|---|---|
| Induration was found in | 1 | |
| Compression " " " | 5 | |
| Thrombosis " " " | 5 | |
| Infarcts " " " | 6 + 3 | old ones |
| Abscess " " " | 3 | |
| Suppuration " " " | 1 | |
| Gangrene " " " | 5 | |
| Atelectasis " " " | 3 | |

*Respiratory System continued:*

| | Cases. |
|---|---|
| Emphysema was found in | 21 |
| Fibrosis " " " | 2 |
| Anthracosis " " " | 4 |
| Healed tuberculosis was found in | 21 |
| Tubercular cavities were " " | 6 |
| Metastasis was " " | 1 |

*Circulatory System:*

| | Per cent. |
|---|---|
| Acute pericarditis | 34 cases, or 17.4 |
| It was fibrinous in | 23 " " 11.7 |
| " " serous " | 11 " " 5.6 |

12 cases, or 6.1% of pericarditis occurred in right consolidation
6 " " 3.0% " " " " left "
16 " " 8.2% " " " " double "

| | Cases. |
|---|---|
| Chronic pericarditis in | 7 |
| Cardiac hypertrophy " | 31 |

The heart weighed over 300 gms. in 37 other cases; in 10 of these over 400 gms. Of all these cases there was sufficient cause for hypertrophy independent of the pneumonia in 24 cases, or 11.7%, leaving 34 cases, or 17.3%, without apparent etiology.

Clotted blood was found in the heart cavities in over 89 cases, or 44.7%, it being distended in 24 cases, or 11.7%.

*Valvular Affection:*

| | | |
|---|---|---|
| Acute endocarditis of the mitral valve in | 2 cases | |
| Acute endocarditis of the aortic valve in | 2 " | |
| Ulcerative endocarditis of the aortic valve in | 6 " | or 3.0% |
| Acute endocarditis of the tricuspid valve in | 2 " | |
| Chronic mitral disease in | 18 " | |
| Chronic aortic disease in | 14 " | |
| Other valves in | 4 " | |
| The myocardium showed degenerative changes in | 18 " | or 9.0% |
| Chronic fibrous myocarditis in | 7 " | |
| Fatty heart in | \ " | |
| Brown atrophy in | 3 " | |
| Arterio-sclerosis present in | 45 " | or 23.0% |
| Aneurism in | 6 " | or 3.0% |
| Fibrino purulent mediastinitis in | 4 " | or 2.0% |

*Gastro-intestinal System:*

| | | |
|---|---|---|
| Gangrenous stomatitis in | 1 case | |
| Ulcerative glossitis in | 1 " | |
| Acute thyroiditis in | 1 " | |
| Acute duodenitis in | 1 " | |
| Acute enteritis in | 7 cases, | or 3.5% |
| Hæmorrhagic colitis in | 3 " | |
| Ulcers of intestine in | 9 " | or 4.0% |
| Appendix abscess in | 3 " | |
| Acute peritonitis with apparent cause in | 4 " | or 2.0% |
| Degeneration of the viscera in | 78 " | or 40.0% |
| Chronic passive congestion of the viscera in | 22 " | or 11.2% |
| Acute splenic tumor in | 74 " | or 37.9% |

4 others present of independent cause.
9 others each weighing over 300 gms.

Liver necrosis in ..... 10 cases, or 5.1%
Gall stones in..... 7 "
Typhoid fever in..... 7 "
Tubercular peritonitis in..... 6 "

*Genito-urinary System:*

Acute nephritis in..... 8 cases, or 4.1%
Trigonitis in ..... 1 case

*Osseous System:*

Acute arthritis in..... 1 case

In brief, from an analysis of these 195 cases of pneumonia, pathologically, we find that the right lung is involved about 4 times oftener than the left, and that there is some double involvement in nearly half of the fatal cases. On the right side the middle lobe is attacked about one-half as often as the upper and lower lobes which are nearly equally affected. There are many more cases of complete than partial consolidation of the lobes. There was complete consolidation on the right in 10.7% of the cases. On the left the lower lobe was affected twice as often as the upper. Left-sided complete consolidation occurred in 5.7% of the cases. In the double pneumonias all combination of lobes were present, the most common being both lower lobes in 18 cases, or 21.6%.

Gray hepatization was somewhat more common than red and mixed hepatization was still more frequent. The double pneumonias showed more red hepatization on the left and the gray on the right.

In three-fourths of 144 cases the remaining portion of the lung tissue was described as congested or œdematous. In 14% it was normal, dry, or crepitant.

The pleural condition was noted in 164 cases, being normal only in 9 cases, or 5.4%, the remaining number showing a fibrinous condition. The exudate was especially thick in 29 cases, or 17.6%, and and was serous in the same number.

The bronchi were injected in 87% of 156 cases.

The bronchial lymph glands were congested in 68 of the 70 cases in which their condition was noted.

The principal associated lesions were as follows:

Acute meningitis occurred in..... 4.0% of the cases
Bronchopneumonia " " ..... 9.2% " " "
Pulmonary thrombosis " " ..... 2.5% " " "
Pulmonary gangrene " " ..... 2.5% " " "
Acute pericarditis " " ..... 17.4% " " "

Fibrinous in two-thirds of the cases, sero-fibrinous in one-third of the cases.

It occurred in equal frequency in right and left consolidation, being slightly more frequent in double pneumonias.

Cardiac hypertrophy, without apparent cause, was found in 17.5% of the cases.

| | | |
|---|---|---|
| Auricles distended by clotted blood in | 11.7% | of the cases |
| Acute endocarditis, one or more valves in | 2.0% | " " " |
| Ulcerative endocarditis (aortic) in | 3.0% | " " " |
| Mediastinitis in | 2.0% | " " " |
| Acute enteritis in | 3.5% | " " " |
| Acute peritonitis in | 2.0% | " " " |
| Visceral degeneration in | 40.0% | " " " |
| Acute splenic tumor in | 37.9% | " " " |
| Liver necrosis in | 5.1% | " " " |
| Acute nephritis in | 4.1% | " " " |

It might be of interest to note that acute endocarditis was associated with acute meningitis in 4 out of 10 cases.

# THE LEUCOCYTES IN ACUTE LOBAR PNEUMONIA.

By J. A. CHATARD, M. D.,

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The leucocytes in the blood may be considered from two different points of view: as protectors of the body during disease, either they may inhibit the infection before it has had time to pervade the body, or after a severe infection, by increasing largely in numbers in the circulating blood, they may kill the germs.

Thus in a great variety of diseases a marked leucocytosis is the body's response to any infection. This is best seen in some of the acute febrile diseases, and often in scarlet fever, diphtheria, and rheumatic fever, but especially in acute lobar pneumonia the most active leucocytosis takes place. In many cases it is so marked as to help in the differential diagnosis of this disease. In no other febrile disease do we find ordinarily so high a leucocytic count. We must bear constantly in mind however, that in the two other prevalent diseases, malaria and typhoid fever, if the disease runs a normal course without complications, a diminution of the normal number of leucocytes usually is found.

The marked leucocytosis of pneumonia has been much studied since its discovery. Virchow and Nasse, followed later by Sorenson, Boeckman, Tumas, Hayem, Limbeck, Billings and many others have all written articles on this subject.

Boeckman, in 1881,[1] laid especial stress upon the presence of a leucocytosis in most acute febrile diseases, except typhoid fever.

Limbeck[2] pointed out the relation between the leucocytosis with the severity of the disease; the fall in the number of leucocytes with the crisis; the absence of a fall during the pseudo-crisis, and that the leucocytes precede and are a part of the inflammatory exudate and that in non-exudative diseases there is no leucocytosis.

Rieder[3] drew attention to the fact that the number of the leuco-

[1] Deutsch. Archiv f. klin. Med., Bd. XXIX, 481.

[2] Ztschr. f. Heilk. Bd. X, 392.

[3] Beitrag z. Kentniss d. Leucocytose, Leipzig. 1892.

cytes depended more on the intensity of the infection and the resistance of the patient than on the degree of fever and the extent of the exudate.

The results of the studies of this subject up to the present time are as follows: Leucocytosis is present in almost all acute infections with the notable exceptions of uncomplicated typhoid fever and malaria; the average leucocytosis in pneumonia is about 24,000 per cmm.; the number of leucocytes diminishes rapidly with the crisis, but more slowly by lysis; a pseudo-crisis is not usually accompanied by a fall in the leucocytes; with delayed resolution, or when a complication is present, the leucocytosis persists; a leucocytosis below 10,000 may mean only a mild case, but usually indicates lack of resistance on the part of the patient, and therefore is a bad prognostic sign. In the differential count of the leucocytes, the polymorphonuclear neutrophiles are usually found to predominate (80-90%), and when this increase is above 90% the prognosis is unfavorable (Löper). There is a relative diminution in the number of lymphococytes.

### Analysis of the Leucocytosis in 582 Cases of Pneumonia.

During the course of the pneumonia an estimation of the number of leucocytes was made in 582 cases. Table I shows the number of cases of pneumonia each year in which the leucocytes were estimated, and the number of times a leucocytosis of a certain degree was reached; in most cases the maximum estimation of all the counts during the day is noted.

To make this table clearer Chart I should be studied with it. Here the solid line indicates the total number of patients having leucocytoses in blocks of 5000, beginning with the lowest number of 2500 per cmm. and passing to the maximum of 105,000 per cmm. It can be seen at a glance that more than half of the patients (about 350) had a leucocytosis of between 15 and 35,000, and nearly one-third (about 198) between 20 and 30,000. The broken line represents the mortality for each advancing series of 5000 leucocytes. The mortality is high when the leucocytes are below 10,000 per cmm., but steadily decreases and is lowest when the leucocytes are between 20 and 30,000. Between 30 and 60,000 the mortality is higher, but remains at a fairly constant line; above 60,000, however, there is a decided rise in the mortality, but it must be remembered that there is but a small number of cases with such

TABLE No. I.

| Years. May. | Leucocytes. 0-5,000 | 5-10,000 | 10-15,000 | 15-20,000 | 20-25,000 | 25-30,000 | 30-35,000 | 35-40,000 | 40-45,000 | 45-50,000 | 50-55,000 | 55-60,000 | 60-65,000 | 65-70,000 | 70-75,000 | 75-80,000 | 80-95,000 | 95-100,000 | 100-105,000 | 105-110,000 | Total. | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1889-90 | | | | | | | | | | | | | | | | | | | | | | R. |
| " " | | | | | | | | | | | | | | | | | | | | | | D. |
| 1890-91 | | | | | | | | | | | | | | | | | | | | | | R. |
| " " | | | | | | | | | | | | | | | | | | | | | | D. |
| 1891-92 | 0 | 1 | | 0 | | 1 | | | | | | | | | | | | | | | 2 | R. |
| " " | 1 | 0 | | 1 | | 0 | | | | | | | | | | | | | | | 2 | D. |
| 1892-93 | 0 | 1 | 1 | 1 | | 0 | 1 | | | | | | | | | | | | | | 4 | R. |
| " " | 0 | 0 | 0 | 0 | | 1 | 1 | | | | | | | | | | | | | | 1 | D. |
| 1893-94 | 0 | 3 | 2 | 3 | 4 | 0 | 2 | 1 | | 1 | | | | | | | | | | | 16 | R. |
| " " | 1 | 0 | 0 | 1 | 1 | 1 | 1 | 0 | | 0 | | | 1 | | | | | | | | 6 | D. |
| 1894-95 | 1 | 2 | 1 | 0 | 4 | 6 | 1 | 2 | 1 | | 0 | 2 | | 1 | | | | | | | 21 | R. |
| " " | 0 | 1 | 0 | 3 | 2 | 1 | 2 | 0 | 0 | | 1 | 0 | | | | | | | | | 10 | D. |
| 1895-96 | 0 | 5 | 4 | 2 | 3 | 0 | 0 | 0 | 4 | 1 | | | | | | | | | | | 19 | R. |
| " " | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | | | | | | | | | | | 4 | D. |
| 1896-97 | 1 | 4 | 4 | 4 | 3 | 2 | 1 | 0 | 1 | 0 | | | | | | | | | | | 20 | R. |
| " " | 0 | 1 | 2 | 2 | 1 | 1 | 0 | 1 | 0 | 1 | | | | | | | | | | | 9 | D. |
| 1897-98 | 1 | 2 | 3 | 5 | 3 | 3 | 0 | 2 | 1 | 1 | 1 | | | | | | | | | | 33 | R. |
| " " | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 1 | 0 | 1 | 1 | | | | | | | | | 6 | D. |
| 1898-99 | 1 | 1 | 2 | 7 | 6 | 6 | 4 | 1 | 0 | 1 | 1 | | | | | | | | | | 31 | R. |
| " " | 0 | 1 | 2 | 2 | 0 | 1 | 1 | 2 | 1 | 0 | 0 | | | | | | | | | | 10 | D. |
| 1899-00 | 2 | 0 | 2 | 3 | 4 | 5 | 1 | 1 | 3 | 0 | | | | | 1 | | | | | | 32 | R. |
| " " | 1 | 3 | 1 | 0 | 3 | 1 | 1 | 0 | 3 | 0 | | | | | 1 | | | | | | 14 | D. |
| 1900-01 | 3 | 6 | 11 | 12 | 4 | 6 | 3 | 2 | 1 | 3 | | | | | | | | | | 1 | 52 | R. |
| " " | 3 | 4 | 3 | 2 | 3 | 3 | 3 | 2 | 0 | 1 | | | | 2 | | | | | | | 26 | D. |
| 1901-02 | 0 | 3 | 6 | 10 | 14 | 7 | 6 | 2 | 2 | 2 | 1 | 2 | 1 | | | | | | | | 56 | R. |
| " " | 1 | 3 | 0 | 2 | 2 | 3 | 1 | 0 | 0 | 2 | 2 | 1 | | | | | | | | | 17 | D. |
| 1902-03 | 0 | 0 | 4 | 3 | 13 | 13 | 3 | 3 | 0 | 0 | 0 | | 1 | | | | | | | | 40 | R. |
| " " | 2 | 2 | 3 | 1 | 2 | 0 | 1 | 0 | 1 | 0 | 2 | | | | | | | | | | 14 | D. |
| 1903-04 | 1 | 4 | 3 | 5 | 8 | 5 | 4 | 2 | 1 | 0 | | | | | | | | 1 | | | 35 | R. |
| " " | 2 | 3 | 1 | 1 | 2 | 2 | 1 | 0 | 0 | 0 | | | | | | | | | | | 12 | D. |
| 1904-05 | 1 | 7 | 8 | 4 | 12 | 6 | 5 | 2 | 1 | 0 | | | | | | | | | | | 46 | R. |
| " " | 1 | 4 | 4 | 3 | 2 | 1 | 1 | 0 | 1 | 0 | | 1 | | | | | | | | | 21 | D. |
| 1905-May 05 | 0 | 3 | 7 | 4 | 8 | 3 | 2 | 1 | 1 | 1 | | 2 | | | | | | | | | 32 | R. |
| | 1 | 3 | 3 | 2 | 2 | 1 | 0 | 0 | 0 | 0 | | | | | | | | | | | 12 | D. |
| Recov'd | 2 | 15 | 19 | 66 | 80 | 81 | 46 | 26 | 14 | 16 | 9 | 5 | 5 | 1 | 0 | 1 | 0 | 1 | 0 | 1 | 418 | |
| Died | 3 | 19 | 24 | 22 | 18 | 19 | 18 | 13 | 6 | 7 | 7 | 2 | 2 | 1 | 2 | 1 | 0 | 0 | 0 | 0 | 164 | |
| Total | 5 | 34 | 73 | 88 | 98 | 100 | 64 | 39 | 20 | 23 | 16 | 7 | 7 | 2 | 2 | 2 | 0 | 1 | 0 | 1 | 582 | |

a high leucocytosis from which to calculate the mortality. It is interesting to note that both patients with an extreme leucocytosis of 95 and 105,000, respectively, recovered.

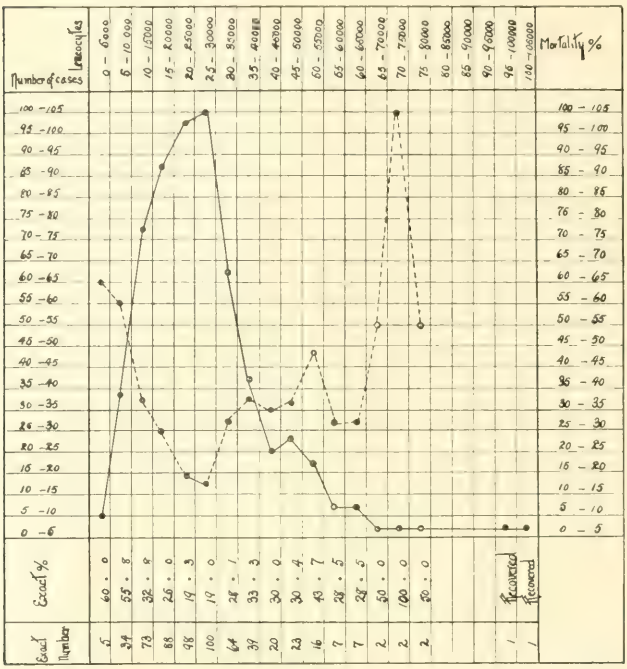


CHART I.

Continuous line represents number of cases of pneumonia.
Broken line represents mortality percentage of same.

*Age.*—On account of the few cases (3) of pneumonia in babies, the effects of leucocytosis in them cannot be estimated accurately, but in the period of from 1 to 5 years, out of a total of 53 patients in which the leucocytes were estimated, no case showed less than 10,000 or

more than 50,000; of these, only 4 (7.5%) died. Three other patients, at this age period, had a leucocytosis of between 50, and 95,000; all 3 recovered.

From 15 years to old age there is a greater range in the number of leucocytes in different cases. There were 202 cases between 20-30 years old, and 178 of them had a leucocytosis of between 10, and 50,000, with a mortality of about 15%; of the remaining cases in this age period, 10 had a leucocytosis below 10,000, with 33.3% mortality, and 14 a leucocytosis above 50,000, with a death rate of 57.1%; in this period fell the case with an extreme leucocytosis (105,000 per cmm.). After 30 years the leucocytosis seems to be less marked, and this is most apparent after 50 years; the mortality in these years with low grades of leucocytosis, is high. Of twelve patients above 55 years of age, with a leucocytosis below 15,000 per cmm. all died.

The relation between age and mortality follows quite closely, as is seen, in the relation between high and low leucocytosis and mortality. Thus, in the period between 1 and 15 years, when according to our statistics the mortality is from 9-10%, the majority of the patients have the most favorable leucocytic reaction; *i. e.*, between 10 and 50,000 leucocytes per cmm., the average being between 20 and 30,000. Between 15 and 30 years, the general mortality is about 19%, but falls to 15% when the leucocytes are between 10 and 50,000 and even lower than this when the leucocytes range from 20 to 30,000. In this age period, however, the lowest and highest leucocyte counts were also met with; at both these extremes the mortality was high, as we have shown. This is the case especially with patients above 50 years of age.

*Sex and Race.*—Among the native white population there were 14 males whose leucocyte count fell below 10,000, of whom 8 died (57.1%). With similar leucocyte counts there were only two females; both recovered. There were 149 males with leucocytes between 10 and 50,000; 38 of them died (25.5%); and 42 females, 11 of whom died (29%). With a leucocytosis of more than 50,000 there were 13 males, with 4 deaths (30.7%), and 3 females with 1 death (33.3%).

Comparing these figures with our total pneumonia mortality statistics, 30.1% male and 32.6% female, no exact deductions can be drawn from either a very high or low leucocyte count in either sex.

Among the negro patients there were 13 males with leucocyte counts below 10,000, and of these 9 died (69.22%). Among the females

only 3 had less than 10,000 leucocytes per cmm., and 1 died (33.3%). There were 159 males whose leucocytes ranged between 10 and 50,000; 35 of them died (22%). Out of 37 females there were 14 deaths (37.8%). With more than 50,000 leucocytes there were 14 males, and 5 deaths (35.7%), and one woman, who died. No inference as regards the leucocytosis can be made from this high mortality among the negro women. Of the foreign born population, there were 6 males with a leucocytosis below 10,000, of whom one-half (50%) died; there was but one woman and she died. There were 108 males with a leucocytosis between 10 and 50,000, of whom 23 died (21.2%); and 17 females with 7 deaths (41.1%). With a leucocytosis above 50,000, there were 5 males, with 4 deaths (80%); and 2 females, with 1 death (50%). From these figures there appears to be no connection between the sex and race, and the grade of leucocytosis or the mortality.

*Seasonal Variation.*—Our statistics show that the majority of the cases of pneumonia occur in the late fall, winter, and early spring months. The mortality in these months does not vary much, and is about the same as the average death rate for the entire year. During the rest of the year, and especially in July and September, the mortality rises markedly, but the smaller number of cases occurring in these months makes it impossible to draw up any accurate statistics. There is no apparent cause for the increased mortality in July and September; the association of typhoid fever with pneumonia in some of the cases does not seem to account for it, as the leucocyte counts in these cases show no essential variations from those of other months. Thus, in March, in which pneumonia is most prevalent (100 cases), and when the average mortality is 28.4%, there was only 1 death (20%) among 5 patients whose leucocytes fell below 10,000; and but 3 deaths (33.3%) in 10 patients with a leucocyte count above 50,000.

Of the remaining 87 patients whose leucocytes ranged between 10 and 50,000, 23 died (26.4%).

In November, when our death rate is lowest, only 18%, 2 out of 3 patients with leucocytes below 10,000 died (66.6%); 5 out of 39 patients with leucocytes between 10 and 50,000 died (13.8%); of these 39 patients, 20 who had a leucocytosis between 20 and 30,000 recovered. There was one fatal case with a leucocytosis of over 50,000 in this series.

Now let us turn to the summer months for comparison. In July the general mortality was about 52%; of 15 patients 7 died, 2 with leucocyte counts below 10,000, and one with more than 50,000; the remaining 4 had between 10 and 50,000 leucocytes per cmm.

In September, of 16 patients, 3 with less than 10,000 leucocytes per cmm. died; each of the remaining 13 had between 10 and 40,000, but among these there were 5 deaths (38.4%). In August there were 5 patients whose leucocytes were below 10,000; but only 2 died (40%). In none of the summer months was there any case of leucocytosis with over 50,000 leucocytes per cmm. There appears, therefore, to be no close connection between the increased death rate of the summer months and the degree of leucocytosis.

*Lung Involvement.*—According to our statistics the right side of the chest was involved in more than half the patients, with a death rate of about 26%. In the vast majority of these patients the leucocytes ranged between 10 and 50,000; it is very striking, however, that when all the lobes were involved the leucocytosis was higher than the average, in fact not one of these patients had less than 10,000, and 12 of the 43 patients showed a leucocytosis of above 40,000; this would seem to confirm the belief that the leucocytes increase in number according to the amount of lung involvement.

The left side, when alone involved, gives the lowest mortality (20%), and here the majority of the leucocyte counts were between 10 and 30,000, as in a total of 99 counts 58 had a leucocytosis between these limits, with only 5 deaths (8.6%).

In apical pneumonia, and when the middle lobe of the right side was alone involved, the leucocytosis was mainly of a mild grade; all of the 6 patients thus affected recovered.

The mortality in double pneumonia was about 39%; in these cases the most common involvement was of both lower lobes. Of 48 such cases 3 had a leucocytosis below 10,000, with 2 deaths; but of 4 with a leucocyte count of 50,000, none died. With the greatest amount of lung involvement (the upper and lower robes of both sides), occurred the highest recorded leucocytosis, 105,000: and about one-fourth of the cases had a leucocytosis above 40,000, with a mortality of nearly 50%; when the leucocytosis fell below 10,000, the mortality rose to 75%.

*Leucocytes and Complications.*—The cases of pleurisy with pneumonia were so common that it is difficult to compare them with the

uncomplicated pneumonia cases in reference to the leucocytosis. Pleurisy seemed to increase the average leucocytosis of pneumonia and tended to prolong its presence. Pericarditis and pneumonia showed a mortality of 88%; 9 of the 31 patients had leucocyte counts below 15,000, and of these 7 died (77%); the remaining 22 patients all had leucocyte counts below 55,000, and 18 of them died (81.8%). The mortality of empyema and pneumonia was 22.2%; 19 of the 24 patients with this complication had a leucocytosis above 20,000; the leucocytosis did not fall below 10,000 in any of these cases. In meningitis, which was always a fatal complication, the average leucocytosis was fairly high; no count gave less than 10,000 leucocytes per cmm. The same was true of endocarditis, which as a complication of pneumonia gave a death rate of about 76%. It is needless to give the exact statistics of all complications (the list is a long one); a milder or severer grade of leucocytosis was present in all. Delirium alone, from its grave prognosis, must be mentioned, and as evidence of extreme toxæmia may be worthy of a word or two. Its mortality was about 45%. Of 13 delirious patients with leucocytes below 10,000, 9 died (69.2%), and of 11 with leucocytes above 50,000, nearly 50% died. In the remaining cases with delirium, the leucocytosis ranged between 25 and 30,000.

*Defervescence.*—The association of the fall in the number of leucocytes and the temperature gave some interesting figures; thus there were 7 instances in which the leucocytes decreased by 5000 during the crisis; 25 by 10,000; 16 by 15,000, and 8 by 20,000; all of them were true crises (a drop of not less than 3 degrees in 12 hours or less). With a protracted crisis (when the temperature falls to normal or below in 12-24 hours) the fall in leucocytes was in 9 cases 5000; in 19, 10,000; in 9, 15,000; in 5, 20,000.

As a rule the fall in the number of leucocytes begins just before the fall in temperature and is quite rapid in a true crisis; but if the crisis is protracted at all, the leucocytes fall gradually and even slower than the temperature (ex: Chart II). Often the continued height of the leucocyte count even after the temperature is dropping may aid in the diagnosis of some complication not yet manifest. In pseudo-crises the fall in leucocytes varies: in some cases following the temperature curve quite closely; in others the fall seems to occur independently of the fall in temperature. In lysis the fall is usually slow and follows the temperature curve closely.

*Prognosis and Mortality.*—In conclusion we may sum up our results as follows:

Of all the acute febrile diseases, lobar pneumonia seems to be accompanied by the greatest increase in the white cells of the blood, or in other words by a marked leucocytosis. This usually varies

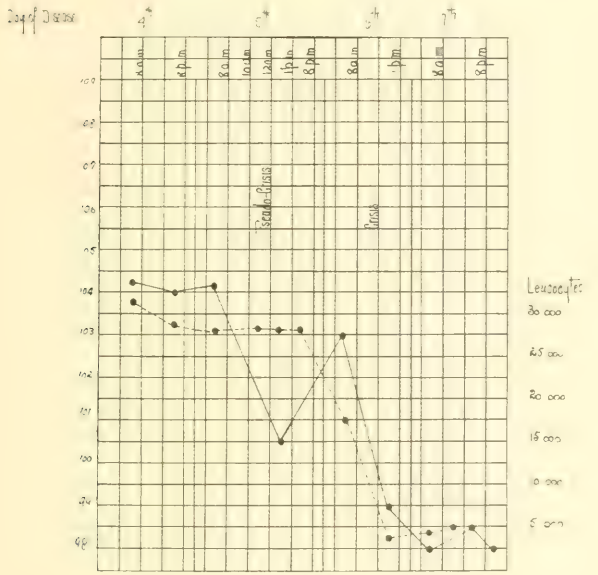


CHART II.

Continuous line represents number of cases of pneumonia.
Broken line represents mortality percentage of same.

between 15 and 40,000, and in most uncomplicated pneumonias ranges from 20 to 30,000.

A leucocytosis below 10,000 may mean either a very mild attack or, as is more often the case, a severe one with little reaction on the part of the patient; it is therefore often a bad prognostic sign. A leucocytosis may mean a good reaction or indicate the presence of

one or more complications; it is not necessarily of bad prognostic import, as many other factors, such as age, vitality of patient and complications must be taken into account.

*Age.*—As regards the influence of age on the leucocytic reaction, the best response seems to be under 30 years of age and less marked above it.

*Sex and Race.*—The leucocytic reaction seems to be better marked in men than in women.

*Seasonal Variation.*—The increased mortality during the summer months seems to have no definite connection with the grade of leucocytosis.

*Lung Involvement.*—An extreme leucocytosis seems to bear some relation to the amount of lung tissue involved, but aside from this, none to prognosis or to mortality.

*Complications.*—The influence of complications on the leucocytes seems mainly manifested by a higher degree of leucocytosis.

*Defervescence.*—The fall in the number of leucocytes follows quite closely the fall of the temperature curve, beginning to decrease a little before a crisis, but rapidly with a true crisis and more slowly in a protracted crisis or lysis. The persistence of a leucocytosis after the temperature has fallen may be of value as a sign of some hidden complication.

Finally the leucocyte count, especially when the leucocytosis is very marked, may be of great value in the differential diagnosis of pneumonia from other acute febrile diseases.

# AN ANALYTICAL STUDY OF TERMINAL PNEUMONIA.

By J. A. CHATARD, M. D.,

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The frequent termination of many of the chronic heart, lung, kidney, constitutional, and other diseases with a pneumonia, whether of the lobular or lobar variety, is a most interesting fact; and in our series of 658 patients with acute lobar pneumonia there were 35 (5.3%) patients in whom this condition was found. In all the pneumonia was of the lobar type, the clinical diagnosis being verified by post-mortem examination in 24 of the 35 patients.

*Associated Diseases,* with a pneumonia as the terminal event, occurred in the following frequency:

| | |
|---|---|
| Cardio-vascular system: | |
| Myocarditis | 5 |
| Arterio-sclerosis | 4 |
| Aortic insufficiency | 3 |
| Mitral insufficiency | 2 |
| Mitral and aortic insufficiency | 3 |
| Aneurism | 2 |
| Thrombosis of external jugular | 1 |
| Total | 20 |
| Renal system: | |
| Chronic nephritis | 9 |
| Diabetes mellitus | 3 |
| Uræmia | 2 |
| Total | 14 |
| Pulmonary system: | |
| Tuberculosis | 2 |
| Bronchiectasis | 1 |
| Total | 3 |

Acute articular rheumatism, typhoid fever, and chronic alcoholism were associated twice each with a terminal pneumonia; while per-

nicious anæmia, cholelithiasis, gangrenous stomatitis, ulcerative colitis, cerebral tumor, gastritis, malaria, and lastly, tubercular peritonitis, were so associated but once. In some instances two or more of the lesions in different organs were present in the same patient.

*Nationality and Sex.*—Among the 35 patients 29 were male and 6 female. Eighteen patients were native Americans; 8 Negros; 4 Germans; 3 Irish; 1 Pole, and 1 Bohemian.

*Age.*—The average of all the patients was about 46.5 years.

*Year.*—The yearly number of "terminal pneumonias" was as follows:

| Year. | No. of cases Act. lob. P. | No. of cases Term. P. |
|---|---|---|
| 1900 | 79 | 6 |
| 1901 | 78 | 5 |
| 1904 | 69 | 4 |

Each of the remaining years averaged from 1 to 3 terminal pneumonias These figures seem to point to a certain correspondence between the two forms of pneumonia in the frequency of their occurrence, but it seems hardly likely that there should be any real relationship between the two, and in any case our figures are too small to make accurate deductions from them.

*Monthly Variation* is seen in the subjoined table:

| | Terminal pneumonias. |
|---|---|
| January | 5 |
| February | 5 |
| March | 4 |
| April | 2 |
| May | 1 |
| June | 2 |
| July | 1 |
| August | 2 |
| September | 4 |
| October | 4 |
| November | 4 |
| December | 1 |

With the exception of the relatively small number in March and December, the terminal pneumonias seem to show the same monthly variations as the acute lobar pneumonias.

*Occupation.*—Twenty-seven patients were employed in heavy, severe out-door labor; this may in part account for the cardiac and renal

diseases which terminated in pneumonia. Only 8 were employed in lighter in-door work.

*Habits.*—Twenty patients (about 60%) used alcohol; 11 moderately and 9 heavily; 7 of these were steady drinkers, and 5 others denied the use of alcohol. Five were moderate smokers, 7 heavy smokers and 3 denied the use of tobacco.

*Previous Diseases.*—Pneumonia heads the list, being noted in the past history of 9 patients. Seven had suffered from cardiovascular disorders; 5 from rheumatism; 2 from typhoid; and 2 from nephritis.

Before the present illness, 10 patients had been in bad condition, 10 in a fair condition, and the remaining either not complaining at all, or in good health. About 5 patients had been exposed to bad weather.

*Leucocytes.*—The maximum count in 22 patients was as follows:

| | | | |
|---|---|---|---|
| 4 | Patients | below | 10,000 |
| 5 | " | between | 10,000–15,000 |
| 2 | " | " | 15,000–20,000 |
| 2 | " | " | 20,000–25,000 |
| 2 | " | " | 25,000–30,000 |
| 1 | " | " | 30,000–35,000 |
| 1 | " | " | 35,000–40,000 |
| 0 | " | " | 40,000–45,000 |
| 2 | " | " | 45,000–50,000 |
| 2 | " | " | 50,000–55,000 |
| 1 | " | " | 75,000–80,000 |

Nine of the patients had a leucocytosis below 15,000, which, as is seen in the general statistics, is a somewhat bad prognostic sign. It was noticeable that in the terminal pneumonias the leucocyte counts were lower than in the acute lobar pneumonias.

*Involvement.*—The right side (54.2%) was attacked more frequently than the left (17.1%). The left lower lobe was affected only 5 times, whereas the right lower lobe was involved 7; the left upper and lower lobes only once.

| Lobes. | |
|---|---|
| Right lower | 7 |
| All lobes, right side | 4 |
| Right upper | 3 |
| Right lower and middle | 2 |
| Right upper and middle | 2 |
| Right upper and lower | 1 |
| Total | 19 |

*Double pneumonia* occurred in 28.5%.

| Lobes. | |
|---|---|
| Right and left upper | 3 |
| Right upper and left lower | 3 |
| Right upper and lower and left upper and lower | 1 |
| Right upper and left upper and lower | 1 |
| Right, all lobes, and left lower | 1 |
| Right lower and left upper and lower | 1 |
| Total | 10 |

*Urine.*—Albumin was present in 31 patients; a heavy trace in 12, a trace in 13, and a faint trace in 6 patients. Casts were present in 15; sugar in 3; bile in 4; and the diazo reaction in 2. In 2 patients in whom the chlorides were determined they were much diminished in amount.

*Complications.*—Dry pleurisy was present 17 times, 10 times on the left side and 7 times on the right side. Pleurisy with effusion occurred once, and was on the right side. Acute endocarditis occurred 4 times; pericarditis 2; meningitis 2; conjunctivitis, abscess of the lung, jaundice, and herpes were each present once. Delirium was present in 9 patients, but in one the delirium may have been partly due to alcohol.

*Treatment*, as in acute lobar pneumonia, was mainly symptomatic and stimulative (strychnine, digitaline, alcohol, codeia, etc.). Hydrotherapy in one form or another was used in about one-half of the cases.

*Conclusions.*—Terminal pneumonia (lobar type) is a somewhat frequent occurrence in chronic diseases, especially of the cardio-vascular and renal systems.

The older a patient, the more liable he is to develop a terminal pneumonia, as his cardio-vascular or renal system is likely to be weak as a result of his age.

The winter and spring months show the largest number of cases. Alcohol is an important factor in the development of the disease. Leucocytosis is less marked than in acute lobar pneumonia.

The ordinary complications of acute lobar pneumonia are apt to be severe. The mortality is high, because of the age of the patients and of their preceding illness.

The development of the disease is like that of acute lobar pneumonia.

# THE TERMINATION OF PNEUMONIA IN CASES WITH RECOVERY.

By CHARLES P. EMERSON, M. D.,

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Pneumonia is a disease interesting from many points of view, but from none is it more so than in the manner of its termination. One would hardly expect that a disease could present a course so constant, and a termination so dramatic. The prognosis in pneumonia varies much. It depends on the general physical condition of the patient and especially on his age, his habits of work and the amount of alcohol he is accustomed to drink. In general hospital practice only from 60 to 80% recover. In private practice from 80 to 94%, while in German army, composed of picked young men, 96.4% recover. And yet, whatever the age and the physical condition of the patient, the course is, in a case with recovery, remarkably constant.

Pneumonia is the very type of a self-limiting disease. It is the best illustration of a disease terminating by crisis. Cases with recovery may end by crisis, in which case the temperature falls from about the level of the fastigium to normal or below in 12 (some say 18) hours or less; they may end by protracted crisis, in which case it reaches normal in from 12 to 14 (others say 18 to 36) hours; while others end by lysis; that is, for the temperature to reach normal requires more than 24 (others say more than 36) hours. The cases with recovery terminating in empyema or in gangrene or abscess of the lung and also the fatal cases do not interest us in this paper.

We use the above definitions of crisis, protracted crisis, and lysis, since these are the time limits usually given. And yet the mere time required for the temperature to reach normal is actually a less important feature than are the clinical symptoms of the defervescence. In a case ending by crisis, suddenly the patient begins to get well. He is very ill, the temperature high, the pulse rapid, the respirations quick and labored, the cough often distressing, the leucocytes high and the prospect for recovery perfectly unknown. Suddenly the temperature falls, the pulse slows and the respiration becomes slower and

easier. In 12 hours or less the difference is remarkable. The patient although very weak, feels much better and the distressing symptoms of pneumonia are gone. In a few hours, with all the appearance of collapse, the patient suddenly passes from a condition of suffering and danger to one of comfort and comparative safety.

In cases with protracted crisis the improvement is quite sudden, beginning at a definite hour, and is progressive. And yet the fall to normal is not accomplished in twelve hours, and the transition is much gentler, much less like collapse. If the case terminates by lysis it is hard to tell just when improvement does begin, and just when normal temperature is reached, so gradually is the change accomplished.

In the above descriptions we have considered the subjective symptoms and the clinical signs, but not the pulmonary physical signs. By means of these last is the process of resolution followed and this it would seem is only rather indirectly connected with the phenomena of crisis or lysis.

We have studied with reference to the manner of termination the records of 112 cases of pneumonia with recovery and without complications or sequelæ which have in recent years been treated in the medical wards of the Johns Hopkins Hospital. In 35 the case terminated by crisis, in 35 by protracted crisis and in 42 by lysis. We would emphasize the relatively seldom occurrence of true crisis, so many medical students seem to learn from text books that crisis is the only proper way for a case to end.

In the above classification we use the temperature as the chief criterion since it is the most rigid; and yet one should not be too rigid in the application of this one test. There can be little doubt that in many clinics the majority of the cases we have classified in the second group would be considered as cases ending by crisis, since clinically the transition from the febrile stage to convalescence was quite sudden.

Of the 10,105 cases collected by Musser and Norris (Modern Medicine, 1909), 4718 or 53.1% ended by crisis. These authors would call a crisis a fall to normal in 18 hours, and perhaps rightly, but we prefer to limit the term to the very abrupt falls since in these cases are the changes in blood, urine and circulation especially striking, and from the study of these undoubted cases ending by sharp and less sharp crisis and by lysis we can draw a clear clinical picture of the groups.

The crisis is one of the most characteristic features of pneumonia and is the most remarkable single phenomenon of this disease. In the

majority of cases it comes between the fifth and the tenth days. In very few cases it has occurred before the third day. "It very rarely occurs after the 12th day."

Several cases of two days' course have been reported. Simon (München med. Wchnschr., 1908, No. 35) saw two such cases; Engels and Pollatashek (München med. Wchnschr., 1908, No. 4) mention several; Musser and Norris give 0.02% as the relative frequency of cases with the crisis on the first day, 0.6% with it on the second, 3.8% on the third, 5.5% on the fourth, 15.9% on the fifth, 14.2% on the sixth, 21% on the seventh, 13.1% on the eighth, 10.5% on the ninth, 5.2% on the tenth, 3.7% on the eleventh, etc. These figures are derived from the study of 4718 cases ending by crisis.

It will be seen that by far the most of the above cases terminated by crisis on the seventh day. The preference for other odd days is not borne out by these figures, contrary to a belief which has been handed down to the present day from the times of Hippocrates.

It has been urged that we cannot be sure that these cases of pneumonia of brief course, clinically of the acute lobar type, are due to infections by *Diplococcus lanceolatus*. It is said that these may have been cases of pseudolobar pneumonia, the lesions of infections by some less virulent organism, as the bacillus of Friedländer. This possibility must be considered since there is always difficulty in determining the organism in a case with recovery.

Of the 35 cases with sharp crisis we have studied, the ages were:

| | Cases. |
|---|---|
| 1-10 years | 9 |
| 11-20 " | 10 |
| 21-30 " | 10 |
| 31-40 " | 4 |
| 42 " | 1 |
| 86 " | 1 |

In 32 of these cases the drop came on the

| | Cases. |
|---|---|
| 3d day in | 1 |
| 5th " " | 4 |
| 6th " " | 4 |
| 7th " " | 5 |
| 8th " " | 3 |
| 9th " " | 9 |
| 10th " " | 3 |
| 11th " " | 1 |
| 12th " " | 2 |

That of these 35 patients 25 were males and 10 females need not surprise one since that is about the proportion of the sexes of patients with this disease admitted to the Johns Hopkins Hospital.

Not even in malaria does one see such a prompt and rapid drop of temperature. The usual time for the fall is from 5 to 12 hours, but

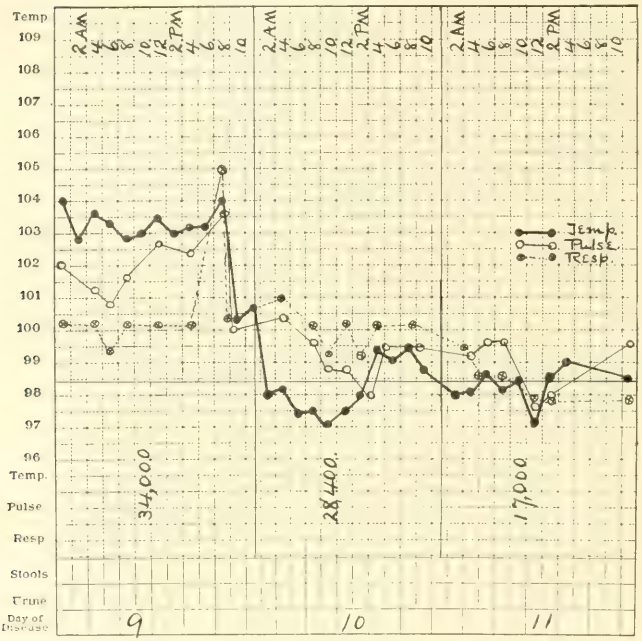


CHART I.*—Male, 19 years old. Simple crisis. The large figures below are the leucocyte counts.

* In this and the following charts the heavy line with black dots represents the temperature curve, the fine line with circles the pulse, and the dotted line the respiration curve. The scale of the temperature is given. For the other scales the space for one degree is that for 10 heart beats and for 5 respirations. The line of 100° = 100 pulse = 35 respirations.

Samuel West saw in one hour a fall of 6° or 8° F., and Jurgensen reports a case with a fall to normal in 4 hours.

In 110 cases (Musser and Norris) the crisis took

| | Cases. |
|---|---|
| 12 hours in | 45 |
| 24 " " | 25 |
| 36 " " | 40 |

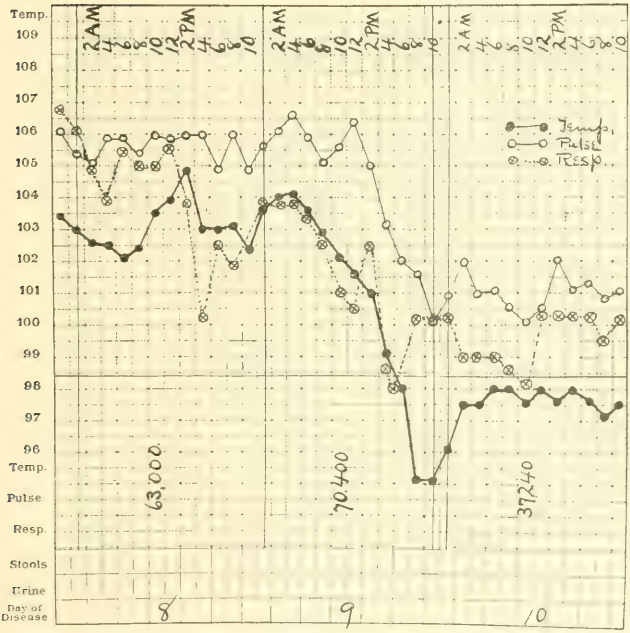


CHART II.—Male, 2 years old. Crisis in the case of an infant, showing the deep drop and high leucocyte counts. (See Chart I, foot-note, page 106.)

Others say the crisis continues

12 hours or less in from 15% to 49% of the cases.
12 hours to 24 hours in from 21% to 37% of the cases.
24 hours to 36 hours in from 8% to 29% of the cases.

The time required in our 35 cases for the temperature to fall to normal was 12 hours or less in most of the cases. In some the fall continued through more than 12 hours, but in these cases it started from a much higher point and fell to a point two or three degrees below normal.

The point from which the crisis began in 35 cases was:

| | Cases. | Cases. |
|---|---|---|
| 106° F. and fractions | 1 | |
| 105° " " | 3 | *1** |
| 104° " " | 7 | *5* |
| 103° " " | 9 | *2* |
| 102° " " | 7 | |

I am inclined to believe that the rapidity of fall is more important than the duration of the fall, and that some cases in which the fall to normal takes less than 12 hours are not truly cases ending by crisis, but the fall was from a relatively low point, while in other cases an abrupt fall took more than 12 hours since the temperature had far to fall.

For instance in 25 cases there was a sudden fall of from 4° to 8.5° F. The rate of fall was

| | Cases. |
|---|---|
| 2.0° F. per 1 hour in | 2 |
| 1.0° " 1 " " | 3 |
| 0.9° " 1 " " | 2 |
| 0.7° " 1 " " | 4 |
| 0.6° " 1 " " | 4 |
| 0.5° " 1 " " | 3 |
| 0.3° " 1 " " | 7 |

The distance of the fall in 35 cases was

| | Cases. |
|---|---|
| 3.5° F. in | 1 |
| 4. ° " | 6 |
| 4.5° " | 4 |
| 5. ° " | 5 |
| 5.5° " | 4 |
| 6. ° " | 5 |
| 6.5° " | 1 |
| 7. ° " | 4 |
| 7.5° " | 2 |
| 8. ° " | 1 |
| 8.5° " | 1 |
| 9. ° " | 1 |

* The figures in italics in this and all succeeding tables are for children of 10 years of age and younger.

A subnormal temperature often follows the crisis. The temperature may drop to as low as 96° or 97° F. This postcritical hypothermia may continue for several days. When prolonged it indicates physical exhaustion. In 35 cases ending by sharp crisis the temperature at the end of the crisis was:

| | Cases. |
|---|---|
| 98.6° F. to 98.9° F. in | 7 |
| 98. ° " 98.5° " | 10 |
| 97.6° " 97.9° " | 4 |
| 97. ° " 97.5° " | 6 |
| 96.6° " 96.9° " | 3 |
| 96. ° " 96.5° " | 3 |
| 95.6° " 95.9° " | 1 |
| 95. ° " 95.5° " | 1 |

In some cases it falls to a still lower point on the following day.

In debilitated persons there may be a critical fall of temperature just before death, but more frequently there is an ante-mortem rise.

Along with the critical fall of temperature is a critical fall in the pulse rate. This fall is not nearly as spectacular as is that of the temperature. It is slower as a rule and continues for two or three days after the temperature has reached normal. It does not as a rule start from a very high point, since pneumonia in the young and strong is not a disease causing much tachycardia.

In 24 cases the pulse before the fall varied from

| | Cases. |
|---|---|
| 140 to 150 in | 1 |
| 130 " 140 " | 3 |
| 120 " 130 " | 5 |
| 110 " 120 " | 4 |
| 100 " 110 " | 5 |
| 90 " 100 " | 5 |
| 80 " 90 " | 1 |

The fall of pulse rate began before that of the temperature in 10 cases, exactly with the temperature in 9, and after the temperature in 14. The lowest pulse rate usually occurs on the second or third day after the crisis.

Our lowest record was 52 (in this case the rate was 100 before the crisis). The lowest rate recorded in 24 cases was, from

| | Cases. |
|---|---|
| 50-60 in | 4 |
| 60-70 " | 4 |
| 70-80 " | 9 |
| 80-90 " | 5 |
| 90-100 " | 2 |

In the above table we have omitted infants and children under 10 years of age. It will be seen that a bradycardia similar to that following typhoid fever does not follow pneumonia ending by crisis.

The rapidity of respiration is very difficult to determine. The rate is so easily influenced by will, by temporary conditions, etc., that in studying the records later it is difficult to tell whether a temporary rise in the curve was an accident or due to the pneumonia. One must be content with general averages of several successive records. Acute lobar pneumonia is of all diseases apt to be accompanied by dyspnœa. Omitting the possibility of an especially acute pleurisy disturbing the rate, the rapidity of respiration usually reaches its maximum between 12 and 36 hours before the temperature begins to fall. Of 33 cases the maximum came two days before the crisis in at least 5; in 7 other cases, it came the day before the crisis; and in only 3 cases did it occur at the beginning of the crisis.

The maximum rate in cases over 10 years of age in 27 cases was

| | Cases. |
|---|---|
| 60 per minute in | 1 |
| 40-52 " " " | 7 |
| 36-43 " " " | 13 |
| 28-36 " " " | 5 |
| 24 " " " | 1 |

In the majority of cases the frequency of respiration begins to diminish before the temperature. It fell more slowly in 16 of these 32 cases, reaching its lowest point one or two days after the crisis. And yet this lowest point is not normal, but slightly faster than normal. During the day after that on which the crisis occurred the lowest rate in 30 cases was

| | Cases. |
|---|---|
| 16 per minute in | 1 |
| 18 " " " | 2 |
| 20 " " " | 11 |
| 24 " " " | 14 |
| 28 " " " | 1 |
| 34 " " " | 1 |

In 11 cases the fall was practically parallel to that of the temperature, in 3 cases the respiration reached a maximum after the temperature had begun to fall, and in 4 cases there was no especial change in the rate of respiration at the crisis.

There is no constant change in the blood pressure with the crisis. A critical fall is rare. Ten cases were studied with this point in view. The age of all was below 30 years. On the day of the crisis, the lowest record was 88 mm. Hg. (15 years old) and the highest 132 mm. Hg. Of the other cases there were 4 below 100, and 4 between 120 and 100. The changes in blood pressure were remarkably slight.

The blood at the time of the crisis presents several interesting features. Its specific gravity is lowered even to 1052 or 1049. This is true in some cases throughout the whole course of the disease, crisis and all (Patella: Congrs. di med. int. Pisa, 1901). The red blood count is often rather high, due perhaps to temporary concentration of the blood. It is said to drop during the crisis and in a few days to return to normal. The leucocytes often rise just before the crisis and are sometimes then at their highest. In the differential counts there is an absence of eosinophile cells, myelocytes and mast-cells. With the drop in fever there is a fall in the percentage of polymorphonuclear neutrophile cells which may continue until these cells equal the small mononuclears.

With or soon after the fall in temperature the eosinophile cells reappear and may rise to 5% or 6% of the total count (Cabot). The reappearance of these cells while the fever is still high is a good sign of the approaching fall of temperature. The appearance of myelocytes may precede or accompany the crisis. These cells may after the temperature is normal rise to 11% of the total count. Mast-cells usually reappear in one or two days after the crisis. The iodophilia disappears in one or two days after the crisis.

Potter and Krumwiede (J. Infect. Dis., 1907, Vol. 4, p. 601) found that the opsonic index falls before the crisis and rises during and after it.

The leucocytes on the day of crisis were, in the 30 cases:

| | | Cases. | Cases. |
|---|---|---|---|
| From | 10,000-15,000 | 4 | |
| " | 15,000-20,000 | 6 | *3* |
| " | 20,000-25,000 | 4 | *3* |
| " | 25,000-30,000 | 4 | |
| " | 30,000-35,000 | 2 | |
| " | 35,000-40,000 | 2 | *1* |
| " | 70,400 | | *1* |

Of 28 cases in only 5 did the leucocytes fall to 10,000 or below on the second day.

Of 19 other cases,

| | | | | | | |
|---|---|---|---|---|---|---|
| In | 3 and 2 | they | were | normal | on | the 3d day. |
| " | 5 | " | " | " | " | " 4th " |
| " | 3 | " | " | " | " | " 6th " |
| " | 1 and 1 | " | " | " | " | " 7th " |
| " | 1 | " | " | " | " | " 8th " |
| " | 1 | " | " | " | " | " 10th " |
| " | 1 | " | " | " | " | " 12th " |
| " | 1 | " | " | " | " | " 15th " |

In two they were not followed to the normal point.

The statement is often made that there is a drop in the count of the red cells just after the crisis, due to destruction of these cells by the toxin of the disease. The often present jaundice and urobilinuria are given as further evidence of hæmolysis. Others say this drop is due to the dilution of the plasma by tissue lymph, which dilution is the result of general peripheral vascular dilatation.

Of 12 cases four showed evidence of blood destruction since there was a reduction of the count which persisted for from three to 12 days after the crisis.

In the eight other cases the fall, if it did occur, must have been temporary since the count from three to eight days after the crisis was practically the same as before.

*Diplococcus lanceolatus,* which can be isolated from the blood in almost all cases of pneumonia (Hoke: Ztschr. f. Heilk, 1908, S. 98; Wiens: Ztschr. f. klin. Med., 1908, Bd. 65) may continue to circulate in the blood even after the crisis. (Borissoff: Wratsch, 1908, No. 18; and Deutsche klin. Wchnschr., 1908.)

During the febrile period the urine seldom exceeds 1000 cc. in amount in 24 hours. There is usually a reduced amount of a highly-colored concentrated urine. Attempts to increase this by forcing the intake of water are often useless. In some cases there is almost perfect anuria for even three days. These cases may recover. An epicritical polyuria is sometimes observed, but not of the grade often seen after typhoid fever.

Garnier and Sabaracanu (Compt. rend. Soc. biol., Vol. 56, p. 1032), found that during the pneumonia the body weight, in spite of the re-

duced diet, remained unchanged or even rose slightly. This can be explained only by the retention of water. With the epicritical polyuria there is a slight loss in body weight.

During the fever the urine is strongly acid, but after the crisis there is marked epicritical decrease of this acidity, and (Pick: Arch. f. klin. Med., 1900, Vol. 68, p. 13) the urine may become amphoteric or even alkaline. The diacidphosphates are reduced from 20 to 40% of the total phosphates to from 5 to 20%. This reduction in the acidity is not due to an increase of carbonates or to ammonia, but to an increased output of the sodium and potassium absorbed from the exudate. In a pneumonic lung in the stage of gray hepatization, there is of $Na_2O$ 5.925 gm. (normal 1.121 gm.) and of $K_2O$ 1.237 gm. (normal 0.092 gm.). It is possible that other retained alkalis which are also then excreted aid to decrease the acidity of the urine.

Of all the urinary features the reduction of the chlorides, first demonstrated by Redtenbacher and since then studied by very many, has attracted most attention. The reasons for this are that this feature is so marked, is so unusual in other conditions, and the early claim, not at all borne out by experience, that the reappearance of the chlorides was a reliable early sign of an approaching crisis. This reduction in the output during the febrile period is due to a chloride-retention of about 2 gm. a day, or an average total retention of 29 gm. In some cases the urine is for a few days practically free of demonstrable chlorides, in other cases there is a reduced output of varying degree; but a considerable reduction is an almost constant feature.

The figures given by Musser and Norris are based on the study of 436 cases:

| | | | |
|---|---|---|---|
| Chloride output | unchanged | in | 19.2% |
| " | " | decreased | " 53.2% |
| " | " | absent | " 27.5% |

The chlorides were followed in but 7 of our cases; they were much reduced in all, but in none to the zero point.

The minimum came:

In 2 cases on the day of the crisis
In 1 case before the crisis
In 3 on the day after the crisis
In 1 on the 3d day after the crisis

The minimum was:

| | Cases. |
|---|---|
| 0.3% in | 1 |
| 3.8% " | 1 |
| 1.5% " | 1 |
| 0.9% " | 1 |
| 1. % " | 1 |
| 2. % " | 1 |
| 0.4% " | 1 |

The increase in the output begins usually about the time the temperature begins to fall, sometimes slightly before, but more often just after. The curve of the output rises slowly during the following three to five days. There is said to be a postcritical excessive output, but this must be rare. Usually the elimination of retained chlorides is distributed over so long a time that on no one day is the output above normal limits.

Of 25 cases whose urine was free of chlorides 28% died. Of 139 cases with reduced chloride output 15.8% died; while of 56 cases with normal chloride output, only 12.5% died.

According to most observers the curve of the chloride output has no prognostic importance. The number of times that the increase of the output heralds a crisis is certainly small. As a rule the retention continues after the crisis (v. Hösslin: Deutsches Arch. f. klin. Med., 1908, Bd. 93, H. 4).

The degree of retention depends on as yet unknown factors. It does not seem to depend on the height of the fever, on the amount of consolidation or on the sometimes present albuminuria. But it is much more marked during the defervescence of cases ending by crisis than in those by lysis.

The evidence is in favor of a defective renal permeability which seems almost specific for the chlorides. The output of other salts, of sulphates for instance, is slightly increased, and while the output of the phosphates also is diminished the postcritical rise of this acid does not always coincide with that of the chlorides and nitrogen. The reduction in the output of phosphates affects especially the earthy phosphates. At or just after the crisis comes a sharp rise in the curve. (Gourand: Compt. rend. Soc. biol., 1902, Vol. 54, p. 373.)

Soon after the beginning of defervescence the output of nitrogen begins to increase and is a good criterion of the absorption of the exu-

date. In cases with delayed resolution treated with X-rays the sudden increase in this output is evidence of the activating influence of these rays on the ferment activity in the exudate. (Edsall and Pemberton: Am. J. Med. Sc., Feb., 1907.)

Maltose was present in the urine of two pneumonia patients. (Rosenberger: Deutsche med. Wchnschr., 1906, Vol. 32, p. 994.)

There is often albuminuria during the febrile period (Blumberg: (St. Petersb. med. Wchnschr., 1907, p. 203) found albuminuria in 88% of all cases). But as a rule this disappears with the crisis and often, interestingly enough, several days before this. This might indicate that renal trouble is a feature of the onset. In some cases the amount of albumin and the casts would suggest an acute nephritis and yet all clears up before the crisis. This was true in two of our cases. There would seem to be some question as to the nature of this protein in the urine. In some cases at least it is not all serum albumin. Lenoble found "protalbumose," while Lochbihler (Zentralbl. f. inn. Med., 1902, Vol. 23, p. 776) found it to be nucleoproteid, protalbumose, heteroalbumose, or deuteroalbumose.

There is often a precritical rise or "critical perturbation" of temperature of 1 to 2° F. at which time it may reach even 107° F. It is sometimes hard to tell whether this rise means crisis or death. A precritical rise of temperature was seen in but 5 of 33 cases and was slight in all of the 5 cases. An antecritical rise of leucocytes was seen in 5 cases. Only one patient showed both of these features.

It is the common opinion that patients with pneumonia are sickest just before the crisis; that is, that the temperature, pulse and leucocytes are highest at this time and the general condition worst.

The temperature after the crisis does not always remain at or below normal, but at once or in one or two days rises and continues elevated for eight or ten days. It rose again and remained irregularly elevated in 14 out of 33 cases; for

| | Cases. |
|---|---|
| 1 day in | 1 |
| 2 days " | 5 |
| 3 " " | 3 |
| 4 " " | 2 |
| 5 " " | 2 |
| 21 " " | 1 |

The leucocytes remained elevated in 20 of 28 cases. In 15 of these cases they were followed until they reached normal. This was in:

| | Cases. |
|---|---|
| 2 days in | 2 |
| 3 " " | 3 |
| 4 " " | 3 |
| 5 " " | 3 |
| 6 " " | 1 |
| 9 " " | 1 |
| 11 " " | 1 |
| 13 " " | 1 |

In the majority of cases with persistent fever or temperature or both, the signs of consolidation were slow in disappearing. In this case either temperature or leucocytes or both may persist, but a slight leucocytosis would seem the most delicate sign of delayed resolution. In delayed resolution the fever may persist for two or three months.

Occasionally cerebral symptoms appear immediately after the crisis. In 6 of 239 cases a definite critical psychosis developed, while in 4 of 150 cases a postcritical psychosis appeared in from three to ten days after the temperature had reached normal (Pohlmann).

Westphal's sign, the absence of the knee-kick, is sometimes noted. Of 12 cases this returned in 6 cases on the day of the crisis, on the next day in 4 and on the second day in 2.

Splenic enlargement often indicates a severe attack. Rychner studied 616 cases with a mortality of 25.7%. Of our cases with enlarged spleens 55.4% died and only 17.9% ended by crisis.

In some cases (9.8% of 1851 cases) there is a *pseudocrisis,* that is, the temperature falls from 104-105° to 102° F., as if for a real crisis, then at once rises to its previous high point or higher and remains elevated for some hours or days longer. This occurs especially on the fifth or sixth day. In another series of 500 cases a pseudocrisis occurred in 54. In 29 of these it occurred on the sixth, seventh or eighth day.

In 14 of our 31 cases with crisis a well-marked pseudocrisis occurred within 36 hours of the crisis in 8 cases, within two days in four cases and in one case six days before the crisis. In one case (21 years old) four pseudocrises occurred, on the fifth, sixth, eighth and ninth day of the disease. In this case the real crisis occurred on the 10th day.

These falls in temperature were almost as rapid as the true crises. The range of fall was from:

| | Cases. |
|---|---|
| 3° to 4° F. in | 3 |
| 4° " 5° " | 6 |
| 5° " 6° " | 1 |
| 6° " 7° " | 4 |
| 7° " | 2 |

The fall required:

| | Cases. |
|---|---|
| 4 hours in | 1 |
| 6 " " | 2 |
| 8 " " | 4 |
| 10 " " | 3 |
| 12 " " | 3 |
| 14 " " | 2 |
| 16 " " | 1 |

The rate of fall was:

| | Cases. |
|---|---|
| 0.3° F. per 1 hour | 1 |
| 0.4° " " " | 5 |
| 0.5° " " " | 4 |
| 0.6° " " " | 2 |
| 0.7° " " " | 3 |
| 0.8° " " " | 1 |

The rises following these falls were very rapid. In 10 cases:

| | Cases. |
|---|---|
| 0.5° F. per 1 hour | 3 |
| 1.0° " " " | 5 |
| 2 ° " " " | 2 |

The time consumed for the rise was:

| | Cases. |
|---|---|
| 4 hours in | 6 |
| 6 " " | 2 |
| 10 " " | 1 |
| 14 " " | 1 |

The effect of the pseudocrisis on the leucocytes was a definite drop in 2 cases (a drop of 8000 cells in one case and of 4000 cells in another).

After the crisis the cough becomes much easier and the sputum more easily expelled (a paroxysmal cough suggests pleural exudate). The amount of sputum expelled after the crisis varies much. In some cases it is abundant, in others absent.

With the sudden fall of temperature there is slowing of the pulse and respiration. The symptoms become at once easier and yet there is often no especial change in the local condition of the lungs so far as the physical signs indicate.

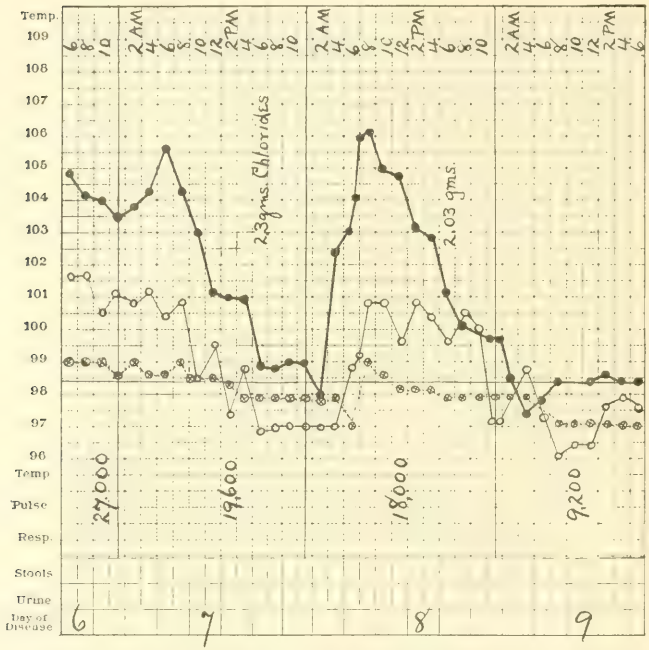


Chart III.—Male, 15 years old. Pseudocrisis on seventh day. (See Chart I, foot-note, page 106.)

*Protracted Crises.* By a protracted crisis we mean that the temperature required considerably more than 12 hours for its fall and yet fell in an almost straight line. In some cases this fall required 48 hours, but the temperature fell continuously and with no remission or only slight remissions.

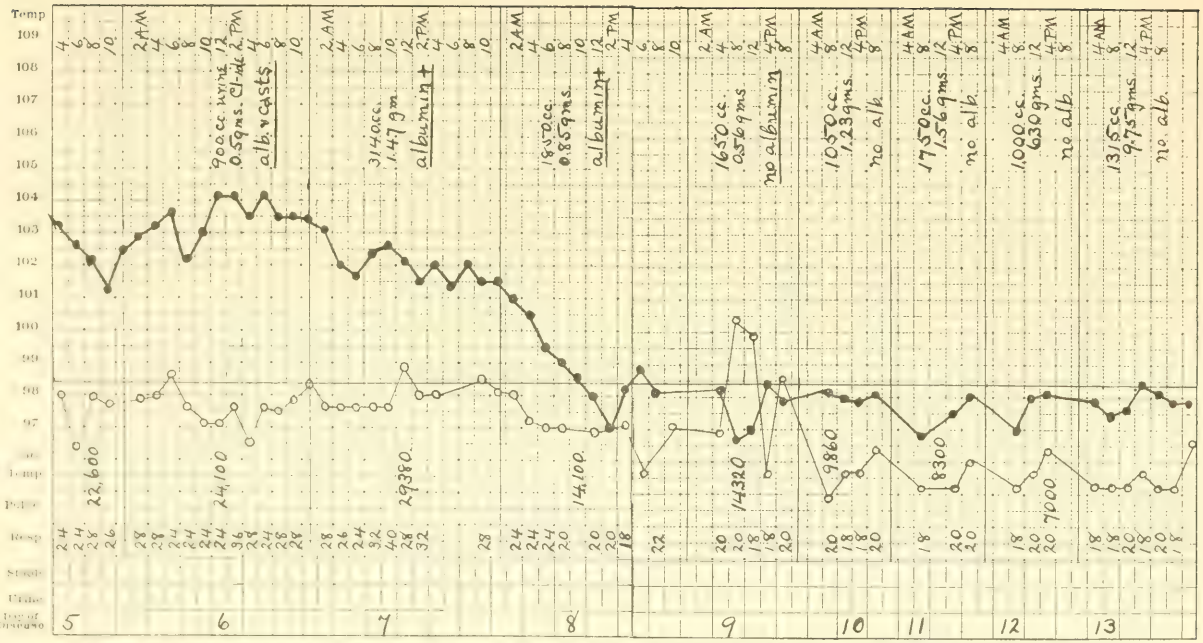


CHART IV. Male, 20 years old. Protracted crisis. Note the urine records above the curve. (See Chart I, foot-note, page 106.)

Clinically these cases differ from the preceding in that the symptoms of the transition from the febrile to the afebrile stage are less intense.

Of these there were 35 cases; 12 females and 23 males. The age distribution of these was:

| | Cases. |
|---|---|
| From 2 to 10 years of age | 6 |
| " 11 " 20 " " " | 4 |
| " 21 " 30 " " " | 16 |
| " 31 " 40 " " " | 7 |
| " 41 " 50 " " " | 2 |

In 29 cases the fall in temperature began:

| | Cases. |
|---|---|
| On the 4th day in | 2 |
| " " 5th " " | 3 |
| " " 6th " " | 5 |
| " " 7th " " | 7 |
| " " 8th " " | 3 |
| " " 9th " " | 2 |
| " " 10th " " | 2 |
| " " 11th " " | 3 |
| " " 13th " " | 1 |
| " " 15th " " | 1 |

The height from which the fall began in 32 cases was:

| | Cases. | Cases. |
|---|---|---|
| 105° F. and fractions in | 5 | |
| 104° " " " | 10 | *3* |
| 103° " " " | 7 | *2* |
| 102° " " " | 2 | *1* |
| 101° " " " | 2 | |

The point to which it fell was:

| | Cases. | Cases. |
|---|---|---|
| 98° F. and fractions in | 14 | *2* |
| 97° " " " | 9 | *4* |
| 96° " " " | 3 | |

The time for the fall was in 32 cases:

| | Cases. |
|---|---|
| 12 to 18 hours | 1 |
| 18 " 24 " | 9 |
| 24 " 30 " | 9 |
| 30 " 36 " | 7 |
| 36 " 42 " | 4 |
| 42 " 48 " | 2 |

The rate of fall in 31 cases was therefore:

| | Cases. |
|---|---|
| 0.35° F. in 1 hour | 1 |
| 0.3 ° " " " | 3 |
| 0.25° " " " | 7 |
| 0.2 ° " " " | 4 |
| 0.15° " " " | 16 |

The maximum pulse rate from which the fall began was in 35 cases:

| | Cases. | Cases. |
|---|---|---|
| 160-169 per min | 1 | *1* |
| 150-159 " " | 1 | |
| 140-149 " " | 2 | *2* |
| 130-139 " " | 3 | *2* |
| 120-129 " " | 7 | *1* |
| 110-119 " " | 9 | |
| 100-109 " " | 2 | |
| 90-99 " " | 1 | |
| 80-89 " " | 3 | |

The fall in 35 cases in pulse rate began before that of the temperature in 12 cases, with it in 10 cases, and after it in 13 cases. In the 32 cases the fall was faster than that of the temperature in 2 cases, parallel in 10, and slower in 20. The maximum pulse rate in 32 cases preceded the fall in temperature in 8 cases, accompanied it in 20, and followed it in 4. The minimum pulse rate in 32 cases preceded the end of the fall in temperature in one case, fell at the same time in 22, and followed it in 9.

The minimal pulse rate in 34 cases was:

| | Cases. | Cases. |
|---|---|---|
| From 110 to 119 per min | | *2* |
| " 90 " 99 " " | | *2* |
| " 80 " 89 " " | 10 | |
| " 70 " 79 " " | 4 | *1* |
| " 60 " 69 " " | 10 | *1* |
| " 50 " 59 " " | 2 | |
| " 40 " 49 " " | 2 | |

Study of these charts shows that a bradycardia is more apt to follow the defervescence by protracted crisis than by sharp crisis.

The respirations run much more parallel to the temperature than does the pulse rate.

The maximum before the fall in rate in 35 cases was:

| | Cases. | Cases. |
|---|---|---|
| 22 per min. | 1 | |
| 24 " " | 1 | |
| 32 " " | 3 | |
| 36 " " | 6 | |
| 38 " " | 1 | |
| 40 " " | 6 | 2 |
| 44 " " | 2 | 1 |
| 46 " " | 1 | |
| 48 " " | 3 | |
| 56 " " | 1 | |
| 58 " " | 2 | |
| 64 " " | 1 | 2 |
| 72 " " | 1 | 1 |

The minimum rate after the crisis in 34 cases was:

| | Cases. | Cases. |
|---|---|---|
| 16 per min. | 3 | 1 |
| 18 " " | 3 | |
| 20 " " | 11 | 4 |
| 24 " " | 7 | 1 |
| 28 " " | 1 | |
| 36 " " | 2 | |
| 40 " " | 1 | |

Of 14 cases the blood pressure remained practically unchanged during the crisis in 9, while a fall occurred in 5. This was slight in 4, but in one case the pressure fell critically from 210 mm. Hg. to 100 mm. Hg. See Chart V.

The pressure at the crisis in 16 cases was:

| | Cases. |
|---|---|
| 85 mm. Hg. | 1 |
| 90-100 " " | 6 |
| 100-110 " " | 3 |
| 110-120 " " | 3 |
| 130-135 " " | 2 |
| 145 " " | 1 |

The leucocyte count on the day when the temperature began to fall in 30 cases was:

| | Cases. | Cases. |
|---|---|---|
| 60,000 cu. mm..... | 1 | |
| 35,000 to 40,000 " " .... | 2 | *1* |
| 30,000 " 35,000 " " ..... | 3 | |
| 25,000 " 30,000 " " .... | 5 | *2* |
| 20,000 " 25,000 " " .... | 7 | |
| 15,000 " 20,000 " " .... | 6 | *1* |
| 10,000 " 15,000 " " .... | 2 | |

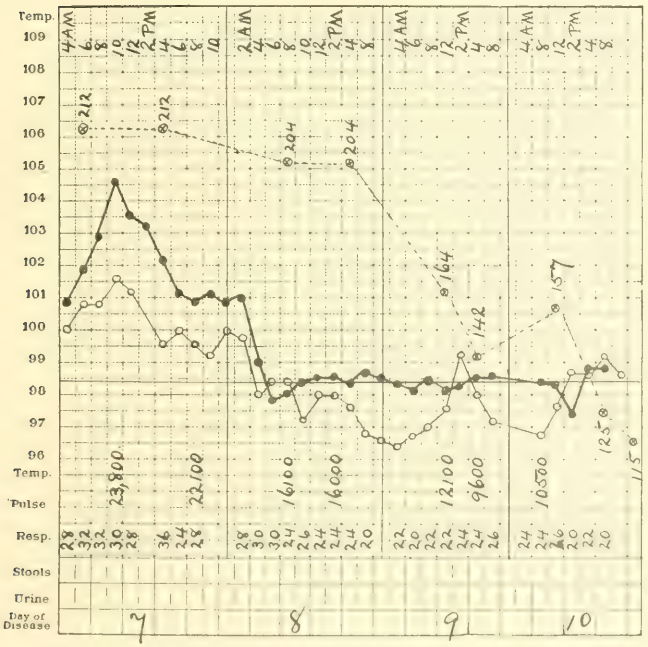


CHART V.—Female, 22 years old. Protracted crisis. Critical fall of blood-pressure. (See Chart I, foot-note, page 106.)

For the leucocytes in 24 cases to fall to normal required:

| | Cases. |
|---|---|
| 1 day in | 1 |
| 2 days " | 5 |
| 3 " " | 2 |
| 4 " " | 2 |
| 5 " " | 2 |
| 6 " " | 3 |
| 7 " " | 1 |
| Over 7 " " | 8 |

Apart from any temporary changes in the blood cell count which might occur at the crisis, there was evidence of no real blood destruction in 13 cases. In 4 the count which followed the crisis was distinctly lower than that which preceded it. Of course there are several reasons why the count might be temporarily high before the crisis (cyanosis, etc.).

The chlorides on the day of the crisis in 12 cases were:

| | Cases. |
|---|---|
| 0 gm. in 24 hours | 1 |
| 0.2 to 0.5 " " " " | 2 |
| 0.6 " 1 " " " " | 2 |
| 1.1 " 1.5 " " " " | 3 |
| 1.6 " 2 " " " " | 3 |
| 2.1 " 2.5 " " " " | 1 |

In five of these cases the chlorides fell to a still lower point on the first or second day after the crisis. The rise of chlorides was slow. In one case eight days after the crisis they had reached only 7 gm.

| | Days. |
|---|---|
| In 1 case they reached 8.2 gm. in | 10 |
| " 1 " " " 10 " " | 5 |
| " 1 " " " 10 " " | 6 |
| " 1 " " " 12 " " | 4 |
| " 1 " " " 16 " " | 6 |

In 4 cases there was albumin in the urine before the crisis. This disappeared on the day of, or the first day after, the crisis.

Of 26 cases in 3 a pseudocrisis occurred before the crisis, but these were only slight, more suggestions of a pseudocrisis than sharp falls like those of the preceding group.

The crisis was preceded by a slight rise of temperature, pulse, etc., in 11 of 28 cases. No trace of this was seen in the other 17. In 6 cases temperature and leucocytes fell to normal on the same day. In

18 cases in which at the crisis the temperature and leucocytes did not fall to normal together, in 8 there was a slight fever or persisting leucocytes. In 8 the leucocytes persisted several days after the temperature was normal, while in only 2 did the leucocytes reach normal before the temperature.

Of 23 cases in 9 the leucocytes had been rising several days before the crisis. They had been falling in 12 and remained about the same in 2.

*Lysis.* In 42 of the cases studied, the temperature fell by lysis; that is, required more than one day to reach normal. Of these 34 were males and eight were females.

The distribution of their ages was as follows:

| | Cases. |
|---|---|
| From 1 to 10 years of age | 5 |
| " 11 " 20 " " " | 10 |
| " 21 " 30 " " " | 19 |
| " 31 " 40 " " " | 6 |
| 56 | 1 |
| 67 | 1 |

In 37 cases the fall in temperature began on the

| | Cases. |
|---|---|
| 2d day in | 1 |
| 4th " " | 2 |
| 5th " " | 4 |
| 6th " " | 8 |
| 7th " " | 3 |
| 8th " " | 6 |
| 9th " " | 5 |
| 10th " " | 2 |
| 11th " " | 1 |
| 12th " " | 2 |
| 14th " " | 1 |
| 15th " " | 1 |
| 16th " " | 1 |

The point from which the fall began was in 41 cases:

| | Cases. | Cases. |
|---|---|---|
| 101° F. and fractions | 1 | |
| 102° " " | 5 | 1 |
| 103° " " | 10 | 1 |
| 104° " " | 16 | 1 |
| 105° " " | 2 | 1 |
| 106° " " | 2 | 1 |

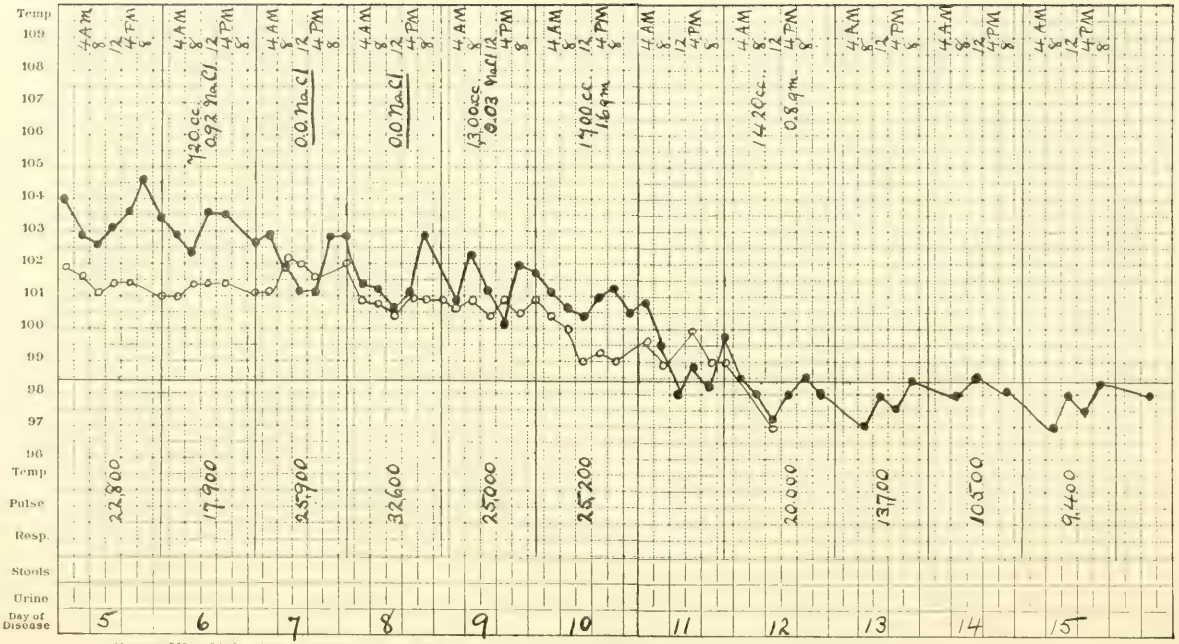


CHART VI.—Male, 37 years old. Lysis. Note the absence of chlorides in the urine. (See Chart I, foot-note, page 106.)

The time required for the fall was in 38 cases:

| | Cases. | Cases. |
|---|---|---|
| 2 days | 2 | |
| 3 " | 11 | *1* |
| 4 " | 6 | *1* |
| 5 " | 6 | *1* |
| 6 " | 1 | *1* |
| 7 " | 1 | *1* |
| Over 7 " | 6 | |

In 17 of the above cases the temperature remained slightly elevated for several days after it had touched normal.

The maximum pulse rate at the time of the lysis in 40 cases was:

| | Cases. | Cases. |
|---|---|---|
| 160-169 | 2 | |
| 140-149 | 1 | *2* |
| 130-139 | 7 | *2* |
| 120-129 | 5 | *1* |
| 110-119 | 10 | |
| 100-109 | 6 | |
| 90-99 | 2 | |
| 80-89 | 2 | |

The fall in pulse rate in 40 cases began before that of the temperature in 6 and *1**; with that of the temperature in 26 and *2**, and after in 4 and *1**.

The minimal pulse rate in 32 cases was recorded before the fever had come to normal in 2 cases, at the same time in 22 cases, and after in 8.

The minimal pulse rate in 35 cases was:

| | Cases. | Cases. |
|---|---|---|
| From 92 to 100 in | 1 | *1* |
| " 90 " 89 " | 3 | *3* |
| " 70 " 79 " | 10 | *1* |
| " 60 " 69 " | 10 | |
| " 50 " 59 " | 6 | |

The respirations in 39 cases were at their maximum

Just before the lysis in 2, *1*
" at the beginning in 28, *2*
" after the beginning in 4, *2*

The maximum respiratory rate in 42 cases was:

| | Cases. | Cases. |
|---|---|---|
| From 22 to 28 in | 6 | |
| " 28 " 34 " | 9 | 3 |
| " 34 " 40 " | 4 | |
| " 40 " 46 " | 7 | 2 |
| " 46 " 52 " | 5 | |
| " 52 " 58 " | 3 | |
| " 62 " 68 " | 2 | |
| " 72 | 1 | |

The minimal rate in 33 cases at the end of the lysis was:

| | Cases. | Cases. |
|---|---|---|
| 16 in | 2 | |
| 20 " | 17 | 3 |
| 24 " | 7 | 1 |
| 28 " | 2 | 1 |

The blood pressure in 18 cases at the time of the lysis was:

| | Cases. |
|---|---|
| 75 mm. Hg. in | 1 |
| 80- 90 " " " | 1 |
| 90-100 " " " | 5 |
| 100-110 " " " | 6 |
| 110-120 " " " | 4 |
| 120-130 " " " | 1 |

During the lysis the blood pressure in 16 cases remained constant in 7, rose in 4, and fell in 5.

The leucocyte count at the beginning of the lysis in 31 cases was:

| | Cases. | Cases. |
|---|---|---|
| 75,000 in | 1 | |
| From 45,000 to 50,000 " | 2 | |
| " 35,000 " 40,000 " | 1 | |
| " 30,000 " 35,000 " | 4 | |
| " 25,000 " 30,000 " | 5 | 2 |
| " 20,000 " 25,000 " | 6 | 1 |
| " 15,000 " 20,000 " | 2 | 1 |
| " 10,000 " 15,000 " | 6 | |

For leucocytes to reach normal required in 25 cases:

| | Cases. | Cases. |
|---|---|---|
| 2 days in | 2 | |
| 3 " " | 3 | |
| 4 " " | 2 | |
| 5 " " | 1 | |
| 6 " " | 2 | 1 |
| 7 " " | 4 | |
| Over 7 " " | 8 | 2 |

In 7 of 23 cases the maximum leucocyte count fell on the day when the lysis began, in 10 it preceded, and in 6 followed the beginning of the fall. In 4 cases the leucocytes reached normal and remained so for nearly all counts, before the temperature was steadily at normal.

In 19 (4 of whom were 10 years old or younger) of 26 cases there was no precritical exacerbation of fever, in 7 there was a slight rise of temperature.

In 18 (2 were children) of 22 cases there was no pseudocrisis. In 4 cases (2 were children) there was a suggestive drop in one on the day preceding the lysis, in one case there was a drop of 5° on the third day before the lysis. In one case there was a pseudocrisis on the third and another on the second day preceding the final fall.

Of 20 cases there was no secondary anæmia resulting from the disease in 11, and a very definite drop of the red cells in 9.

*Chlorides.* In cases ending by lysis it would seem that the chlorides reach lower points than in those ending by crisis. Of 12 cases in 4 the urine at lysis did not contain a measurable amount of chlorides. It is of interest that the rise does not begin promptly as in cases ending by crisis, and the minimal may fall considerably after the lysis begins. In one case the chlorides measured 0.3% at the beginning of lysis and for the following 18 days, during which time, however, the patient was not perfectly afebrile. In another case the chloride curve had two minima, one the day before the lysis began (0.8%) and the second four days after the lysis began (0.4%). In 3 cases the minimum fell on the fourth day after the drop began. In the patient who voided 10 gm. on the day lysis began the chlorides for the successive three days were 1, 1.6 and 0 gm.

In 4 of the above cases there was a trace of albumin until the lysis, none after.

*Resolution* usually begins at once with the crisis. In some cases the physical signs of beginning resolution antedate the crisis, in some follow and in others accompany it. In cases with delayed resolution the lungs may not clear up for from one to six weeks. In these cases the temperature may have fallen by lysis to normal and remained there, but usually there will be very slight daily recurrences of fever.

Changes in the exudate which lead to resolution are due to an autolytic digestion by proteolytic enzymes which are present much more abundantly in the exudate of a lung in the stage of gray hepatization

than in the preceding stages. The average weight of the normal lung is 600 gm; that of a solid lung from 1500 to 2500 gm. All of this 1900 gm. excess due to exudate must be liquefied and expectorated or excreted by the kidneys. By following the nitrogen excess in the urine the progress of the resolution may be followed and even an estimate formed of the amount of exudate.

Ascoli and Bezzola (Berl. klin. Wchnschr., 1903, p. 39) found that during the first stage of fever the blood serum of patients with pneumonia was abnormally, strongly antityptic (tested with pancreatic solution and Arthus' No. F.-gelatin). This condition persists for a time at this level and then diminishes often parallel with the decrease of local symptoms. They believe that this increased antikinase power of the serum is a reaction of the organism to the large amount of kinase in the blood and is derived from the destruction of the leucocytes.

Bittorf (Deutsches Arch. f. klin. Med. 91, 212, 1907) studied the distribution of the proteolytic ferments derived from leucocytes and the antiferment found in the urine, blood and sputum in the course of cases of lobar pneumonia. He found in the urine a strong trypsin-like ferment with, or shortly before, the crisis. This can be demonstrated for one or two days. He thinks that this originates from the broken down leucocytes of the exudate. The test for the presence of this in the blood is the decreased inhibitory power of the serum during the crisis. For instance, supposing in a case of pneumonia before crisis five drops of serum were required to check the trypsin action of one drop of pus, during the crisis from 30 to 40 drops of serum might be necessary. (Ascoli and Bezzola: Zentralbl. f. Bakteriol., 1903, p. 783. Pawlow has shown two components of trypsin; the pancreatic juice and the intestinal fluid. The trypsin is active only when these are mixed. The enterokinase, the component from the intestinal fluid, is more powerfully inhibited by human serum than is the pancreatic juice.)

*Delayed resolution.* Many of the cases in the group of those ending by lysis must have been cases of delayed resolution. Very probably there were many other cases in the other two groups. For this reason these cases vary so among themselves that group study is rather difficult. As a rule the liquefaction and absorption of the exudate begins with the defervescence and continues until the lungs are clear, a matter of from three to ten days. But in other cases the lobe or lobes may remain solid for weeks and yet finally clear. Some of these cases have

a typical crisis and the temperature remains normal during the two or three weeks that the exudate persists. In other cases the temperature falls by lysis but remains slightly elevated, perhaps for a few hours each day, for three or four or even eleven weeks that the consolidation persists. In other cases after weeks of fever the patient dies exhausted.

Delay in the liquefaction of the exudate by the ferments liberated by the breaking-down leucocytes is the explanation usually given for and is the idea conveyed by the term, "delayed resolution." But the nitrogen curve would suggest a continuing process, a "chronic exudation."

The question which now interests us is, Can we from the study of these cases get any hint of the reason why one case terminates within a few hours by crisis while the termination of another ending by lysis takes several days?

There are many theories to explain this and these can be divided into two groups. It is possible that the termination depends on the local conditions in the lung. One might think that if at the beginning of the fall of the temperature the exudate in all parts of the consolidated area were in the same stage of advanced gray hepatization then defervescence would be a rapid process; while if with the larger areas of gray hepatization there is present even a small patch of more recent consolidation this latter might determine the fall by lysis. According to this view the condition of the exudate determines also the time of the defervescence. It might be supposed that absorption into the blood stream of certain soluble substances from the softening areas of consolidation would be a sufficient explanation for the drop in temperature.

But there are many objections to all theories like the above. The features of defervescence certainly do not depend on the amount of exudate, for one sees just as spectacular crises and just as tedious lyses in cases with one small area of consolidation as in those with three or four lobes solid. Again, the physical signs do not suggest much relationship between the physical conditions in the solid area and the clinical symptoms of the defervescence. To the clinician the phenomena of resolution and defervescence are little related.

The view now held is that defervescence is evidence of acquired active immunity to the toxin of *Diplococcus lanceolatus*. This idea is the basis of several theories. The prostration, fever, tachycardia and, to a certain degree, the dyspnoea are symptoms of infection by

this micro-organism. It is not at all certain that all, or most, of this toxin originates in the consolidated areas. In practically all cases the condition is also a septicæmia and the relative importance of the local pulmonary condition and this septicæmia are not yet understood. Either may be the primary and more important condition. But toxæmia there certainly is, and the severity of the case depends much more on the relation between the virulence of this toxin and the resistance of the patient to it than it does on actual amount of consolidated lung. Most agree that with the intoxication begins the process of active immunization. It is the method by which this is accomplished which is the disputed point. When at last the immunity has reached a certain point the course of the disease is run and convalescence begins. According to this view the temperature will fall by crisis or lysis according to the suddenness and completeness with which this active immunity is established.

For further discussion of these theories the reader is referred to works on immunity. We mention them since they serve as fitting introduction to our problem, Does the study of the above 112 cases throw any light on the question: Why do some cases end by lysis and others by crisis?

The amount of consolidation is certainly not a controlling factor. The uniformity of the stage of the consolidation may control, but how much it does cannot yet be decided in cases with recovery.

As a general statement it is claimed that termination by crisis is more common in children than in adults and in adults than in the aged. But this statement is not generally accepted and others claim that lysis is the more common termination in children than in adults.

Of our cases the mean age (not the average age, for we refer to that age around which the greatest number of the cases cluster) was 18 years; of those with protracted crises, 25; and of those ending by lysis 24 years. Theoretically one would expect termination by crisis in children since their thermo-regulator mechanism is more unstable than is that of adults. They certainly are subject to greater and more sudden variations in temperature. On the other hand we see sharp crises in patients over 80 years of age. Evidently age is not an all important determining factor. Sex certainly also is not. It is the opinion of many that crisis is more common in strong than weak persons. This opinion is doubtless gained from the study of cases in

which pneumonia complicates chronic diseases. Certainly if one limit the "weakness" to the prostration caused by the pneumonia itself, the opinion of many observers would be, I think, that the sicker the patient the better the chance of a termination by a crisis, granting that the patient recovers.

Again, it is said that crisis is more apt to occur in brief cases than protracted ones. We would question this and ask, If duration has any influence, are not the influences favoring crisis the cause of the brevity of the case, rather than *vice versa?*

In our cases the mean day on which the fall in temperature began in the cases terminating by crisis was the eighth day of the disease; in those ending by protracted crises the seventh day; and in those by lysis the eighth day. Evidently the duration of the fever had little influence over the method of termination. It is probably true that the longer the course the less the chance for a crisis. In our cases with crisis only 3 (9%) continued beyond the 10th day, of those with protracted crisis 4 (17%) and of those with lysis 6 (17%). But this difference is very slight.

There is, we believe, little doubt that the proportion of crises varies much in the various "seasons" of pneumonia. In some years the frequency of cases followed by empyema, *e. g.*, is very surprising.

The next question is, Are the cases ending by crisis more completely "well" after the crisis than are the others? In our cases with crisis there was slight fever for several days in 13 of 33 cases (39%) and a persisting leucocytosis in 20 of 28 cases (71%). Of 24 cases with protracted crisis in only 6 (25%) did the leucocytes and temperature reach normal on the same day and remain there. In the cases ending by lysis, of course, all the cases have slowly falling temperature and leucocyte curves. We may be sure, however, from the above that in over half of the cases with sharp crisis there was some evidence of still active postcritical intrapulmonary trouble.

Our next question is to determine whether the course before the defervescence in any demonstrable way determines the method by which the temperature shall fall; that is, is this method "predetermined?"

Definite pseudocrisis occurred in 14 (40%) of the 31 cases ending by crisis; in but 3 (11%) of the 26 cases ending by protracted crises and there is ground for doubt whether anyone of these deserves to be

called a definite pseudocrisis; while in but 4 (17%) of 22 cases ending by lysis did any fall suggesting a pseudocrisis occur. Yet some of these were very definite critical falls. Evidently the cases ending by sharp crisis show earlier in their course a preference for that method of termination.

Again, is the crisis the method of defervescence in the sickest cases? In these cases is the "contest between life and death" sharper than in other cases? This is a hard question to answer, yet the following points against it may be urged.

The mean temperature from which sharp crises began was just 104° F.; that from which protracted crisis began was 103.6° F., and that from which lysis began was 104.2° F. These figures are practically the same. In the last mentioned group the highest temperatures were found.

The mean pulse rate when the sharp crises began was 115 per minute; when the protracted crises began, 124; and when the lyses began, 122.

The mean respiratory rate (in cases over 10 years of age) when the sharp crises began was 41; when the protracted crises began was 42; and when the lyses began was 40.

The mean leucocyte count at the beginning of the sharp crises was (in patients over 10 years of age) 22,000 per ccm.; when protracted crises began 24,000; and when the lyses began, 25,000.

The mean output of chlorides at the beginning of sharp crises was 1 gm.; of protracted crisis, 1.3 gm.; and of lyses 1 gm. in 24 hours. And yet there was much greater retention of chlorides in the cases ending by lysis than in the others.

It is evident that the conditions as concern temperature, pulse, respirations, leucocytes and chloride-output are practically the same at the beginning of defervescence, whatever be the speed with which the temperature falls.

But is a precritical intensification of these above features more common in one group than in the others? In 33 cases ending by sharp crisis there was an antecritical rise of temperature in 4, of leucocytes in 4, of both in one, of either, therefore, in 27%; in 28 cases ending by protracted crises there was an antecritical rise of temperature in 11 (40%); in 7 of 25 (28%) of the cases ending by lysis there was a slight precritical perturbation of fever.

There is nothing which we have been able to demonstrate in the course of a case of pneumonia which gives us any hint as to how the manner of its defervescence is determined; that is, whether it will fall by lysis or crisis. Evidently the question also belongs to that great problem of immunity of which we still know so little.

But one point is certain "crisis" is more often associated with "shock" or "collapse" than is lysis and there is an element of danger in this method of termination. The relation of this condition to this method of termination is, however, still uncertain.

Crisis is usually accompanied by extreme exhaustion and relaxation; by sweating in 9 of 43 cases; often by irregular, rapid, feeble pulse, often dicrotic and of low tension; by epistaxis; by profound sleep, by polyuria, by occasional incontinence of urine and by diarrhoea. Critical collapse or at least a tendency to it is not uncommon. This occurs sometimes at the beginning of the crisis, but more commonly in the midst of it. It is accompanied by chilliness, cold perspiration, dyspnœa, cyanosis, a weak, rapid, irregular pulse, mental incoherence and subnormal temperature. These patients usually recover, but sometimes death results. And yet the collapse is an incident during the course of the critical fall or immediately following it, and is usually of only a very few hours' duration. A very sharp collapse is usually accompanied by a progressively slowing pulse and respiration. The patient is weak and covered by a profuse perspiration. During the crisis the pulse may suddenly become rapid and the other symptoms of collapse appear.

A good illustration of "critical collapse" or, more properly of "crisis complicated by collapse," is the following (see Chart VII):

Medical No. 22,539. L. T., male, white, age 30. This patient was admitted on the sixth day of a severe attack of acute lobar pneumonia of the right upper and middle lobes. From the sixth to the day of crisis the temperature varied from 104° to 106° F. His pulse rate rose progressively during these days. On the afternoon of the 10th day of the disease the patient became delirious, refused water and nourishment and became excited when anyone approached him. He fought rigorously all attempts to examine him and had to be put under restraint. The crisis began at 8 p. m. on the 10th day. The temperature fell in 12 hours from 104° to 97° F. At this time the delirium subsided. At 6 a. m. on the 11th day the temperature was 98.7° F. and the pulse 88. At 7 a. m. the patient became profoundly collapsed. The deeply jaundiced skin became pale and cold and drenched in sweat. The mucous membranes became cyanotic. He was so deeply unconscious

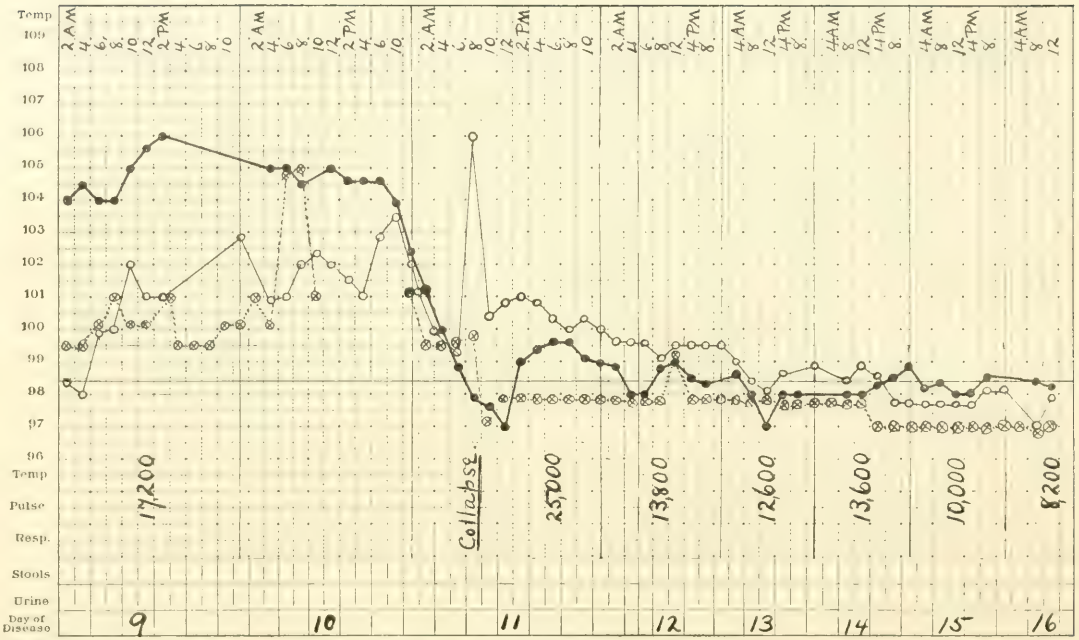


CHART VII.—Male, 30 years old. Crisis with collapse. Note its brief duration, and the precritical evidence that there was danger of collapse. (See Chart I, foot-note, page 106.)

that he was not roused when the infusion needle was inserted. The temperature fell to 97.8° F., the pulse rose to 160 beats to the minute, and became very feeble. Loud, tracheal râles were audible. The patient gradually cleared up under stimulation. There were at this time no changes in the physical signs over the right lung.

In other cases it is even more serious and has resulted fatally. Each medical ward man has his turn at mistaking crisis for fatal collapse and after some experience is willing to treat each crisis as if it were, knowing that the danger at that time is not slight.

Collapse one or two days after the crisis is more grave. This means serious injury to the myocardium. "Even occasional irregularity before crisis results in death" (Mackenzie).

The temperature falling by sharp crisis often reaches a subnormal point, 96° or 97° F. The mean lowest point in the above 35 cases ending by sharp crisis was just 98° F. and in those falling by protracted crisis 98° F. or the same. More very low figures, however, were found in the sharp crisis list (8 of 35 cases fell below 97° F.) than in the list of cases falling by protracted crisis (3 of 32 fell below 97° F.). In those falling by sharp crisis the pulse ran a mean of 75 per minute, in those ending by protracted crisis, 61; and in those ending by lysis, 62. The slightly rapid pulse rate during the few days following the crisis is evidence of slightly greater weakness which these cases show.

# ACUTE ENDOCARDITIS WITH LOBAR PNEUMONIA.

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Acute endocarditis may arise as a complication or sequel of lobar pneumonia, and in this case may be caused either by the pneumococcus or by some other microorganism. Pneumonia may develop during the course of acute endocarditis, from the same or a different germ. The commonest of these combinations will be considered in this article; namely, pneumococcus endocarditis occurring during or after lobar pneumonia.

Endocarditis was described in 1835; Heschl called attention to the condition in 1862; in 1885 Osler laid especial emphasis upon the importance of pneumonia as a cause of malignant endocarditis, having noted its presence in over 25% of his cases of malignant endocarditis; in 1886 Netter reviewed 82 cases. In 1904 Preble collected 132 cases from the literature and reviewed the subject thoroughly. A short review by Thorel also appeared in 1904. One or two cases have been reported during the last two years.

The cases may be classified like other endocarditis cases, either clinically, into simple or benign, and grave or malignant endocarditis: or, bacteriologically, into pneumococcal, streptococcal endocarditis, etc.; or, according to the primary disease, into pneumonic endocarditis, rheumatic endocarditis, etc.; or, according to the heart lesion, into vegetative or ulcerative, valvular or mural endocarditis.

In Preble's 132 cases the endocarditis was recognized clinically in only 0.06% to 0.3%, and was found at autopsy in 3.0% to 16.0% of pneumonias. Taking the average of all statistics published on this subject he finds that endocarditis occurs in approximately 1% of all cases and in 5% of fatal cases. A study of 127 cases of malignant endocarditis showed that 21.2% were caused by the pneumococcus; different investigators finding from 14% to 32%. Streptococci and staphylococci apparently cause malignant endocarditis slightly more frequently than pneumococci.

There is nothing distinctive in the pneumonia which causes endocarditis, nor in the valve changes produced by the pneumococcus. It

is quite common to find delayed resolution, organizing pneumonia, or abscess formation in the lung. Endocarditis seems to be as common with right sided as with left sided pneumonia. The attempt has been made by Kerchensteiner and others to distinguish the endocarditis produced by the pneumococcus from endocarditis due to other bacteria, by anatomical features, but this cannot be done. The infection may involve any of the valves, the mural endocardium or the vessels at the base of the heart. The lesions vary in location and numbers and may present any of the types seen in other forms of acute endocarditis, from small pinpoint vegetations, to shaggy cauliflower growths. Ulceration is common, especially when the aortic valve is affected and may lead to perforation or to rupture of a valve segment, or to gangrene. In probably the majority of cases the vegetation shows organization beginning or advanced, and it is common to find lime salts deposited in even recent vegetations. The early vegetations show the usual structure: a trabeculated framework of degenerating platelets, with red and white corpuscles and fibrin in the interstices. Nests of bacteria are usually met with and foci of softening are not uncommon.

Preble tabulated 141 cases to show the distribution of the heart lesions. The left side of the heart was affected in 82.2% of his cases, the right side in 12% and both sides in 5.7%. He compares these figures with Jürgensen's statistics for endocarditis in general and finds that the right heart is involved in 17.7% of the cases of pneumococcus endocarditis, but only in 5.5% of the cases of endocarditis in general. In Osler's series of malignant endocarditis the right side was envolved in 16% of the cases.

Preble[1] tabulates the heart lesions in endocarditis in general, and in

[1] Preble's figures do not seem to bear out this statement. Adding together the various percentages tabulated, and comparing the figures obtained in pneumococcal endocarditis with Jürgensen's general endocarditis statistics, we have:

| | Pneumococcal Endocarditis. | Jürgensen's Statistics. |
|---|---|---|
| Total involvement of Aortic Valve | 58.0% | 28.0% |
| " " " Mitral | 47.3% | 78.3% |
| " " " Tricuspid Valve | 14.1% | 3.2% |

This indicates that in pneumococcal endocarditis the aortic valve is involved twice as often, the tricuspid more than four times as often, and the mitral something more than half as often as in endocarditis.

the pneumococcal form according to distribution and states that the aortic valve is involved more than twice as often, the tricuspid twenty times as often and the mitral valve only one-third as often in pneumococcal as in other forms of endocarditis.

In Osler's series of cases of malignant endocarditis from all causes, the aortic valve was involved in 45.8%; the mitral, in 57.6%, and the tricuspid, in 0.926%. Acute pericarditis occurs frequently with the endocarditis.

Nearly all cases of endocarditis arising during the course of pneumonia or soon after are caused by the pneumococcus. The pneumococcus was found alone in sixty-four of sixty-nine cases studied by Preble: pneumococcus and streptococcus were found together in three cases, and there was one case each of infection with streptococcus alone and with streptococcus and staphylococcus. A few cases have been reported of pneumococcal endocarditis without pneumonia.

Taking into account the greater frequency with which males are attacked by pneumonia, Preble concludes that women with pneumonia are about twice as apt to be attacked by endocarditis as men are. In Osler's cases of malignant endocarditis from all causes except traumatism and puerperal infection, the percentage of females affected was even higher than in Preble's of pneumonic endocarditis, in the proportion of 38% to 31%. He found that 70.9% of all endocardial complications in pneumonia occurred between the ages of 30 and 60, which is about the same age distribution obtaining in malignant endocarditis in general. Pneumonia itself has a different age distribution, and some other types of endocarditis, such as the rheumatic, are more prone to occur in early life.

Chronic intoxications, anæmia, and a lowered state of health from any previous cause play the same important rôle in pneumonic endocarditis as in other diseases. The proportion of valve complications varies in different epidemics of pneumonia.

In the great majority of cases in which malignant endocarditis arises in pneumonia, examination will reveal the presence of a chronic lesion of the heart. Such a chronic lesion was present in over three-fourths of Osler's, and in about the same proportion of Kelynack's cases. Orth goes so far as to state that infective endocarditis never develops in a heart previously free from disease, but this seems to be an extreme view.

The lodgment of the bacteria upon the valve is supposed to occur in exactly the same way as in other forms of endocarditis; the bacteria being pressed into or between the endothelial cells mechanically by the force of the closure of the valves, or being picked up by the endothelial cells. The vegetations, ulcerations, etc., arise as in other cases of endocarditis. How frequently bacteria are present in the circulating blood during pneumonia has been shown within recent years by blood cultures. Wandl advances an interesting hypothesis to explain the mode of origin of pneumococcal septicæmia and endocarditis. Noting the frequency of late endocarditis, with organizing pneumonia in which the very few bacteria could be found in the lung, he examined the bronchial lymph glands, found them badly infected, and concluded that the pneumococci pass, not directly from lung to heart, but from an infected bronchial gland into the lymphatics and thence to the heart. He thinks this explains the greater frequency with which the right heart is involved in pneumonia. It must be remembered, however, that the right heart is doing more work during an attack of pneumonia than it is at other times, and that this increased work tends to diminish its power of resistance.

The endocarditis and pneumonia may develop so nearly at the same time that it cannot be determined which began first; the pneumonia may pass directly into the endocarditis, or there may be an afebrile interval between the pneumonia and the endocarditis. This is very common. The afebrile period lasts from a few hours up to a week or two. There is nothing characteristic about the onset or symptoms, and the cases may be classified like malignant endocarditis in general, according to the symptom complex, into pyæmic, typhoidal, cardiac, or cerebral types of the disease. To these must be added a milder type of the disease, Preble having one recovery, Axtell reporting a probable case, and three examples being found in our series. The temperature is variable, being usually irregular; the pulse is not characteristic; the leucocyte count gives no information of the endocardial condition. Drenching sweats occur in this as in other forms of malignant endocarditis. The types of disease are illustrated in the cases summarized below. The symptoms are remarkably diverse, and the only features common to most cases are those of an acute febrile infection with fever, prostration, sweating, and frequently delirium. There is nothing constant in the course followed by the disease. The patient may die in a few days from septicæmia, meningitis, or heart complica-

tions, or the case may drag on for months. The average duration is about thirty days, according to Preble.

Various complications may develop in the course of pneumonia with endocarditis. The frequency with which abscess and gangrene of the lung and organizing pneumonia occur has been mentioned. Pericarditis, infarction, and embolism are as frequent as in other forms of endocarditis. Probably the commonest complications are septicæmia and meningitis. Strictly speaking, it seems that all of these cases should be regarded as septicæmias. Meningitis occurs frequently. It was found in eight of 103 pneumonia cases of Osler's, five times being accompanied by endocarditis. Of twenty-five instances of meningitis in his series of malignant endocarditis, fifteen occurred in pneumonia. Meningitis occurred in about 12% of all his cases, being found most often in connection with pneumonia. According to Preble's statistics, meningitis complicates pneumonia in about 30% of cases with no endocarditis, but in 56.6% of cases when endocarditis is present.

In the majority of cases a diagnosis cannot be made by the physical signs, and the heart lesion is not found before death. An endocarditis may be suspected in a prolonged attack of pneumonia upon the supervention of typhoidal, septic, or cerebral symptoms. The development of an irregular fever after the temperature has reached normal is also suggestive. The interval of normal temperature rarely lasts more than a week, usually only a few days. The fact that females between thirty and sixty are relatively more liable to develop endocarditis with pneumonia has been mentioned. Of local signs, systolic murmurs are not important by themselves; a diastolic murmur, not pericardial, is to be looked upon as due to endocarditis. The murmur may grow more intense after its first appearance, or it may appear suddenly and remain unchanged. Frequent blood cultures will often shed light upon perplexing cases. At times the subjective symptoms, or the signs of progressive heart failure, may point to the diagnosis.

The outlook is very grave in pneumonic endocarditis, and the complication usually proves fatal. In rare cases, as in one of Preble's and three of Osler's series, the patient recovers from the acute attack, but, as Preble states, "if an endocarditis develops in the course of pneumonia, it is four to one that it will be of the so-called ulcerative or malignant type." Of the 132 cases analyzed by Preble only four recovered. He is probably correct in believing that more cases recover

than the statistics indicate, or, in other words, that benign endocarditis is more common with pneumonia than it is supposed to be.

The treatment is altogether supportive and symptomatic. Results do not encourage the general employment of antipneumococcal serum.

The records of the medical department of the Johns Hopkins Hospital from 1889 to 1905 include among 658 cases of pneumonia thirteen complicated by acute endocarditis. The following synopsis presents the chief features of these thirteen cases:

No. 1.—Hospital No. 598; white; male; thirty-four years; bartender; admitted September 19; died December 29, 1892. Family history negative; patient used alcohol moderately and gave history of having had rheumatism at the age of eighteen. In 1901 he was treated for mitral stenosis and malaria. The present illness began as an attack of heart failure, the lungs being clear. He had an attack of facial erysipelas from September 30 to October 25. The loss of compensation returned on November 20; ecchymoses appeared in the skin on the 24th; two days later pleurisy developed; he convalesced again, survived a second attack of facial erysipelas (December 2 to 6); on December 24 signs of pneumonia appeared; dyspnœa increased, and he died on December 29. The temperature remained subnormal during the last attack.

Autopsy No. 377. Anatomical diagnosis: acute croupous pneumonia in both lungs with pleurisy and hydrothorax; chronic endocarditis affecting mitral and aortic valves with fresh vegetations on mitral, aortic, and tricuspid valves; adherent pericardium; cardiac hypertrophy; chronic changes in liver, spleen, and kidneys, etc.

Bacteriological examination showed the presence on the heart valves and in lungs of the pneumococcus.

This case presents the features of a chronic endocarditis with secondary chronic changes in other organs upon which became implanted the acute infection erysipelas, acute endocarditis, and terminal lobar pneumonia and pleurisy.

No. 2.—Hospital No. 11,911; black; male; forty-one years; laborer; admitted January 25; died January 26, 1895. Family history, negative; personal history children's diseases; alcohol and tobacco used moderately. Onset of present illness six weeks before admission with hiccough, cough, and increasing weakness; worse for three weeks, with pain on coughing felt in the upper right chest; severe chills every night for one week; no swelling of feet; frontal headache throughout illness; appetite poor; bowels regular; stiffness in right hip for two weeks. On examination an area of dullness and a cavity were found over the right upper front and right scapula; the heart sounds at apex were slightly prolonged; leucocytes 11,300; urine contained numerous hyaline, finely granular casts with traces of albumin; temperature very irregular, ranging between 98.2° and 105.6°. Soon after admission patient became unconscious, Cheyne-Stokes breathing developed, and a loud diastolic murmur was heard trans-

mitted down the right border of the sternum, and heard feebly above the second rib. The aortic second was heard with the murmur. The heart's action was regular and not rapid. A systolic whiff at apex was transmitted to anterior axillary line. The patient died of heart failure.

Autopsy No. 619. Anatomical diagnosis: croupous pneumonia of right lung with multiple abscess formation; acute ulcerative aortic endocarditis with rupture of one segment; chronic fibroid pericarditis; purulent meningitis; cloudy swelling of liver and kidneys; chronic orchitis.

Bacteriological examination: Cultures from lungs showed the pneumococcus, but the cultures from the heart were sterile, though smears showed the presence of the pneumococcus.

In this case a prolonged attack of lobar pneumonia was complicated by abscess formation, and, following this, by ulcerative endocarditis and meningitis. The acute endocarditis developed as a complication during the pneumonia in a heart already the seat of a chronic pericarditis.

No. 3.—Hospital No. 13,571; black; female; fifty years; admitted August 12, died August 25, 1895; family and personal history negative. Present illness began two weeks after severe muscular exertion with pain in the right side, cough, weakness, fever, and loss of appetite; chills for three days before admission. On examination there were the signs of lobar pneumonia of the right upper lobe; the heart was negative, and there was a slightly swollen and painful right shoulder joint. Albumin and hyaline casts were found in the urine; the temperature was very irregular, ranging between 99.5° and 104.8.° No signs of the heart lesion were detected during life. The signs continued to be those of pneumonia until August 21, when, following a chill, the pulse became irregular and rapid, remainso up to death on August 25.

Autopsy No. 714. Anatomical diagnosis: acute vegetative endocarditis of tricuspid valve with chronic endocarditis; acute lobar pneumonia; healed tuberculosis of left apex; chronic adhesive pleuritis; chronic interstitial nephritis; acute splenic tumor; general pneumococcus septicæmia.

Bacteriological examination showed the presence of the pneumococcus in both, the lungs and heart.

In this case a colored woman with chronic thickening of the valves and chronic nephritis developed lobar pneumonia which was followed by acute endocarditis and general septicæmia.

No. 4.—Hospital No. 22,391; white; female; thirteen years; admitted March 23, discharged May 18, 1898. Patient was admitted with pains in the chest and back, and swelling and pain in ankles, wrists, and shoulders. Family history negative; previous history of an attack of rheumatism three years ago followed by chorea. Present illness began with a slight cough, followed three days later by rheumatism in the ankles, extending in twenty-four hours to the wrists and shoulders. On examination there was a very loud, rough, systolic murmur at apex, and a loud pericardial friction with a leathery squeak. The heart dullness beginning at the third rib, extended to a point 5 cm. to the right of mid-

sternal line and 7.5 cm. to the left. Signs of pneumonia were present in the left upper lobe and over a small area in the lower right back. The rheumatism subsided; the pericardial friction continued palpable and audible; a mitral diastolic murmur also developed. The patient convalesced after recovering from a complicating pleurisy. A blood culture taken April 15 was negative. On discharge May 18 the patient looked perfectly well, the heart action was satisfactory, although there was still systolic retraction of the lower left ribs, an enlarged area of cardiac dullness and pericardial friction together with systolic and diastolic murmurs at apex. The patient was readmitted in January, 1900, with diabetic coma, mitral stenosis, and pericarditis, and died in this attack.

In this case, apparently the pneumonia, endocarditis, and pericarditis were complications of a second attack of acute articular rheumatism which possibly had its origin from a mild throat infection. The patient recovered from the acute infections and survived nearly two years, dying from a different disease.

No. 5.—Hospital No. 23,184; white; male; six years; admitted June 17, discharged July 26, 1898. Family history good; past history of whooping cough and a doubtful history of rheumatism. Present illness of two weeks' duration with irregular fever and chills. On examination the left side of the chest was tender, dull on percussion, with harsh and tubular breathing accompanied by many râles; leucocytes 17,000. The pneumonia rapidly improved. When convalescing from pneumonia it was first noticed (June 1) that the first sound at the apex was replaced by a rough murmur and that the pulmonic second was accentuated. The patient left the hospital well, still having the cardiac murmur. In March, 1901, he was readmitted with acute articular rheumatism and mitral stenosis with insufficiency.

No. 6.—Hospital No. 26,417; black; male; fifty-two years; admitted May 6, died May 14, 1899. Was admitted in a semicomatose condition, and no history could be obtained. The chest was flat on percussion over the right front and back, where tubular breathing and various râles were heard; there was a diastolic murmur. The sputum was copious, mucopurulent, brown, not offensive, and separated into three layers on standing. The patient remained semiconscious with rigid muscles; temperature between 99.2° and 101.6°; the leucocytes rising to 26,000. The lung and heart conditions did not change. Lumbar puncture which was negative on May 7 and 10, was positive on May 13, when Kernig's sign was first noted. The patient was apparently improving, but died suddenly on May 14. The urine showed traces of albumin with casts.

Autopsy No. 1362. Anatomical diagnosis: lobar pneumonia of right lung with gangrene; acute ulcerative aortic endocarditis; cardiac hypertrophy and dilatation; acute meningitis; cloudy swelling of liver and kidneys; chronic diffuse nephritis; chronic fibrous myocarditis; arteriosclerosis, etc.

Bacteriological examination showed the presence of the pneumococcus in the heart's blood and on the mitral valve.

In this case the cardiac lesion apparently developed late in the course of lobar pneumonia with gangrene, in a colored man with chronic changes in heart, blood vessels, and kidneys.

No. 7.—Hospital No. 28,363; white; male; laborer; thirty-seven years; admitted November 5, died November 18, 1899. Family history of tuberculosis; personal history of rheumatism six or seven years years ago, very severe for two months; gonorrhea followed by lues ten years ago; patient is a heavy eater, a hard worker, and uses alcohol and tobacco freely. The present illness began six weeks ago with severe cough, dyspnoea, bloody expectoration, and weakness; swelling of ankles for two weeks; cough interferes with sleep. There were signs of loss of cardiac compensation with lobar pneumonia of the right middle and lower lobes together with pleural friction. At the apex a systolic murmur transmitted to the axilla, and a soft diastolic murmur was heard. Systolic and diastolic murmurs were heard at the aortic area, and the pulmonic second was accentuated. The liver was enlarged. On admission tubular breathing was heard over only a small area below right nipple, but this area increased in size and extended well out into the right axilla by November 15. On the 13th the temperature suddenly rose to 105.8°, the patient became unconscious, there was incontinence of urine and fæces; the reflexes were exaggerated, Kernig's sign was present, but there was no rigidity, and once in a while the patient would answer questions. The leucocytes stayed between 9700 and 9800.

Later in the day the patient became rational and complained of severe headache. The leucocytes rose successively to 12,400, on the 16th to 22,400, and on the 18th to 48,000. Lumbar puncture on November 16 showed pneumococci. The same germ was recovered from a purulent discharge coming from the right eye. On the 18th the patient died with œdema of the lungs.

Autopsy No. 1442. Anatomical diagnosis: acute lobular pneumonia and pleurisy; pleural adhesions; pulmonary infarct in right lung; acute ulcerative endocarditis; chronic valvular endocarditis; cardiac hypertrophy and dilatation; arteriosclerosis; thrombosis of superior sagittal sinus; purulent cerebrospinal leptomeningitis; acute purulent panophthalmitis; infarction of spleen; chronic passive congestion; cloudy swelling of kidneys; chronic nephritis.

Bacteriological examination: Vegetation on mitral valve gave the pneumococcus in culture, also the pneumococcus was present in the lung infarct and meningeal exudate.

In this case there are many etiological factors. The family history was bad, the personal history was worse, and there had been a previous attack of rheumatism. In the presence of cardiac, arterial, and renal changes an attack of pneumonia developed. Apparently the acute endocarditis was secondary to the pneumonia, and in its turn gave rise to the meningitis, sinus thrombosis, ophthalmitis, and infarctions of lung and spleen.

This case presented the clinical features of lobar pneumonia, but at autopsy a lobular pneumonia was found.

No. 8.—Hospital number 42,969; white; male; forty-two years; clerk; admitted June 2, died June 9, 1903. Family history negative; personal history, always weakly; pleurisy in 1878; typhoid in 1901. Present illness for one week; for three days has been chilly and feverish with cough and expectoration. On day following admission the sputum was blood-streaked; leucocytes 13,300; patient semidelirious. Lobar pneumonia of the right front, axilla, and back developed. The leucocytes for two days fell to 8100. The tubular breathing was never characteristic over the consolidated area. Four days after admission and three days after the development of pneumonic symptoms, a systolic murmur suggestive of pericardial friction was heard to the left of the sternum. The delirium and tremor increased. Rigidity of the neck developed and Kernig's sign was noted June 8. On June 9 a faint aortic diastolic murmur was heard; pulse, dicrotic and collapsing; blood cultures, negative; urine contained a trace of albumin; temperature, irregular, ranging from normal to 104.5°.

Autopsy No. 2119. Anatomical diagnosis: lobar pneumonia with gray hepatization of right lung; chronic adhesive pericarditis; acute aortic endocarditis with ulceration of aortic leaflet; acute tricuspid endocarditis; fibrous myocarditis; atheroma of aorta and coronary arteries; cirrhosis of liver; chronic interstitial pancreatitis with fat necrosis and abscess formation; chronic nephritis; acute splenic tumor; meningitis; acute arthritis.

Bacteriological examination: no organisms grew.

In this case, a man with chronic changes in heart, blood vessels, liver, kidneys, and pancreas was attacked by lobar pneumonia, from which developed acute endocarditis, meningitis, and arthritis.

No. 9.—Hospital No. 44,236; white; male; forty-six years; admitted October 3, died October 6, 1903. Family history negative; personal history, in bed three weeks with rheumatism sixteen years ago, has had measles, chicken pox, dysentery, malaria, acute urethritis three months ago lasting ten days. Present illness: five days before admission was seized with sudden severe pain in lower part of abdomen with sweating and rapid breathing. The pain has continued, but is less severe; has had slight diarrhea and vomited once. On admission there were the signs of lobar pneumonia in the right back and axilla; the heart sounds were clear; leucocytes 8000. On October 4 a soft systolic murmur was heard at apex of heart. The leucocytes rose to 11,000 on October 5 and the breathing became definitely tubular; the patient sank and died early October 6; urine showed considerable albumin with casts and blood cells; the temperature fell slowly from 104.5° on day of admission to 102° at death.

Autopsy No. 2189. Anatomical diagnosis: cardiac hypertrophy and dilatation; chronic aortic and mitral endocarditis with fresh vegetations on mitral valve; acute lobar pneumonia with gray hepatization of upper right lobe; anthracosis; chronic passive congestion of abdominal organs; nutmeg liver; cloudy swelling of liver, kidneys, etc.

Bacteriological examination: culture did not yield the pneumococcus.

In this case the pneumonia and acute endocarditis developed so nearly simultaneously that there is nothing to indicate which came first. Here again the acute infection was preceded by chronic changes in the lung, heart, and liver.

No. 10.—Hospital No. 45,169; black; male; forty-two years; laborer; admitted January 2, died January 17, 1904. Family history, negative; personal history, in bed nine months with rheumatism in 1885, measles and malaria as a child; works hard and uses tobacco and alcohol. Present illness began with a severe shaking chill four days ago, lasting one day, and accompanied by cough and sharp cutting pains in the right side. This was followed by headache, general pains, and fever. On examination both backs were flat on percussion and the breath sounds were accompanied by fine crackles not altered by coughing; no definite pneumonia; heart clear; leucocytes 22,100; the next day flatness on percussion and tubular breathing were noted at the right base; the heart sounds were clear on January 4; on January 8 patient was delirious; condition was worse, the pulse very weak and soft; the tubular breathing was extending and a pleural friction was very marked over the right lung; the leucocytes were 33,000. The general condition improved for several days, the condition of the lungs remaining unaltered. On January 14 the patient was worse and drowsy; he developed a headache which increased; the leucocytes were variable, on the morning of January 15 being 9600, in the evening 21,200. On January 16 it was noted for the first time that the first sound at apex was preceded by a loud rumbling murmur, and he second sound replaced by a blowing diastolic murmur, which was heard loudly over the tricuspid area and along the left sternal margin; the pulse grew worse and the heart weaker; the patient developed stiffness of the neck, and spinal puncture gave a turbid fluid; blood cultures and cultures from the spinal fluid showed pneumococcus infection; there was a trace of albumin and a few casts in the urine; the patient died on the 17th. The temperature was markedly irregular throughout.

Autopsy No. 2232. Anatomical diagnosis: acute lobar pneumonia with organization; acute ulcerative aortic endocarditis; general pneumococcus infection; infarctions of spleen and kidneys; acute fibrinopurulent cerebral meningitis; old tuberculosis of bronchial lymph glands.

Bacteriological examination: culture did not yield the pneumococcus.

In this case the lobar pneumonia attacked a colored man with a history of rheumatism. General septicæmia developed with endocarditis and meningitis, as complications to the organizing pneumonia.

No. 11.—Hospital No. 45,864; white; male; sixty-five years; admitted March 4, died March 24, 1904. Family and personal history, negative; present illness began four days before admission with a feeling of weariness and a shaking chill, followed by sweating. Chills returned every day after onset and there was coughing and sputum streaked with blood.

The patient had a definite lobar pneumonia with flatness in the right back, tubular breathing and crackling râles. By March 16 the patient

had practically recovered and was up in a wheel chair, though still too weak to walk; the temperature was normal from March 10; the first sound at apex was followed by a soft systolic murmur not transmitted, but audible over the body of the heart. On the night of March 16 the patient suddenly had a chill and rise of temperature, but no change could be made out on physical examination. The dullness over the lower right back did not clear up entirely; no murmurs were heard over the heart on March 20; the temperature was irregular, varying between 101° and 105°; on the 21st of March the patient was somewhat cyanotic and the vessels of the neck collapsed quickly; the systolic murmur at apex again became audible and the second sound was replaced by a diastolic murmur; this murmur developed rapidly and a presystolic rumble also became audible; the general condition was fairly good until the 24th, on which day patient was comatose, the neck stiff, the eyes incoordinate; he rapidly sank; the heart sounds grew fainter up to death; pneumococci were recovered from blood cultures and from the spinal fluid during life; albumin and a few casts were present in the urine.

Autopsy No. 2273. Anatomical diagnosis: organizing lobar pneumonia of right lung; acute lobar pneumonia right and left lungs; acute ulcerative aortic endocarditis; acute seropurulent spinal meningitis; acute splenic tumor; chronic nephritis, etc.

Bacteriological examination: pneumococcus in culture from lung, but not from heart.

In this case lobar pneumonia occurred in a man with chronic changes in the kidneys. The man was extremely ill with pneumonia, but convalesced and was nearly ready to leave the hospital, when there was a sudden development of the acute endocarditis, meningitis, and septicæmia. Although the patient had practically convalesced from the pneumonia, the clinical local signs were still present and the complications were associated with organizing pneumonia.

No. 12.—Hospital No. 50,121; white; male; twenty-two years; tailor; admitted March 4, discharged May 2, 1905; family and personal history good; present illness began two weeks ago with pain about the heart, later moving to the joints, followed by difficulty in talking; no chill; no cough. The illness presented the features of an ordinary lobar pneumonia complicated by aortic insufficiency. He stayed in the hospital fifty-eight days and recovered, leaving with a chronic heart lesion well compensated; the blood cultures were negative; leucocytes varied from 9000 to 23,200; urine was clear. The clinical diagnosis was lobar pneumonia complicated by aortic endocarditis and insufficiency and associated with acute articular rheumatism and mitral insufficiency and stenosis. Dr. Cole, resident physician, made the following note on this case:

"Diagnosis in this case is a little uncertain. At first it was supposed to be malignant endocarditis. Whether the presystolic rumble and thrill were due to a true mitral stenosis, or were Flint murmurs could not be decided, though an organic lesion of the mitral valve seemed likely."

No. 13.—Hospital No. 50,249; white; male; forty-seven years; stevedore; family history, negative; pneumonia twenty-seven years ago; uses alcohol and tobacco to excess; general health good. The patient was admitted for pains in the right knee and left shoulder; no respiratory symptoms developed until the fourth day after admission; pneumonia then became evident and ran a severe course; a pericardial rub was noted about the sixth day; cyanosis and dyspnœa increased steadily; the patient sank and died on the 15th day after admission. The temperature was irregular, ranging between 99° and 105.5°; leucocytes ran from 19,800 to 30,700; traces of albumin and bile were found in the urine.

Autopsy No. 2505. Anatomical diagnosis: lobar pneumonia of left lower and right upper lobes; serofibrinous pleuritis and pericarditis; subacute endocarditis; chronic mitral endocarditis; cardiac hypertrophy and dilatation; acute splenic tumor; cloudy swelling of liver and kidneys; chronic passive congestion.

Clinically this case presented the features of acute lobar pneumonia and pericarditis, developing an acute endocarditis and pleurisy and preceded by articular rheumatism; there was a terminal alcoholic delirium.

The general features of these thirteen cases may be briefly considered:

Etiological Factors: *Age.*—One case occurred in each of the first three decades, one in the fourth, five in the fifth, and one in the seventh decade. The ages of those recovering were six, thirteen, and twenty-two years; the fatal cases occurred after the beginning of the fourth decade. In comparing these figures with those in the general statistics as regards mortality, we may note how low it is in the first three decades, thus, at the age of six the mortality is as low as 5%, at thirteen years about 15%, and at twenty-two years about 17%; it rises steadily to old age. During the fifth decade which showed our greatest loss, the general mortality was about 42%.

*Race and Sex.*—There were nine white and four negro patients; of these thirteen patients, two were females (one white and one colored); all cases among the negroes were fatal; little if anything can be noted in relation to the general statistics on account of the few cases.

*Occupation.*—Laborers, of whom there were six in this series, had a general mortality of about 36%, which is extremely high and indicates somewhat the relation of the previous overwork of the heart, inducing some chronic changes, which will be noted later.

*Season.*—The cases developed at every season of the year; nine of the thirteen began during September, December, March, and April.

*Mortality.*—Of the thirteen cases, ten died and three recovered from the acute infection, a mortality of about 76%.

*Previous Illness.*—There was a definite history of rheumatism in five cases, a doubtful history in two others. The rheumatic attacks occurred three, six, nine, and eighteen years before the final illness.

A previous history of heart disease was obtained in only one case, No. 1. A previous history of pneumonia was obtained in one case, No. 13. No definite history of other respiratory troubles was obtained.

*Onset.*—The disease complex started as pneumonia in nine cases; the first symptoms were those of heart disease in two cases, and in two cases the illness started as acute articular rheumatism.

The duration of the final illness varied from eight days in the rapidly fatal cases, with an average of nineteen days for all fatal cases, up to fifty to seventy days for the cases which recovered.

Of the nine cases starting as pneumonia, seven died. Both of the two cases starting as heart disease died. Two cases started as articular rheumatism, one recovering after a long illness leaving chronic endocarditis; the second dying of endocarditis and septicæmia.

All of the ten fatal cases came to autopsy. Without considering other complications, endocarditis and pneumonia occurred four times; endocarditis, pneumonia, and meningitis, six times.

The clinical notes on the heart conditions may be compared with the autopsy findings:

Case 1. Aortic and mitral endocarditis with loss of compensation; at autopsy, chronic aortic and mitral stenosis; cardiac hypertrophy, acute vegetative endocarditis of aortic, mitral, and tricuspid valves.

Case 2. Prolongation of first sound at apex; later, a systolic whiff from apex to axilla and a loud diastolic murmur to the right of sternum; at autopsy, fibrous pericarditis, acute ulcerative aortic endocarditis.

Case 3. No signs of heart lesion during life; at autopsy, chronic tricuspid endocarditis.

Case 6. A diastolic aortic murmur; at autopsy, fibrous myocarditis; acute ulcerative aortic endocarditis.

Case 7. Systolic murmur at apex transmitted to axilla; diastolic murmur at apex; systolic and diastolic murmurs at aortic area; at autopsy, chronic and acute ulcerative endocarditis of aortic and mitral valves.

Case 8. A systolic murmur to left of sternum, suggestive of pericardial friction, and a faint diastolic murmur most intense at second left interspace; dicrotic, collapsing pulse; at autopsy, ulcerative aortic endocarditis; acute vegetative tricuspid endocarditis.

Case 9. A soft systolic murmur at apex; at autopsy, chronic aortic and mitral endocarditis; acute vegetative mitral endocarditis; cardiac hypertrophy and dilatation.

Case 10. First sound at apex preceded by a loud rumbling murmur, and second sound replaced by a blowing diastolic, heard loudly over tricuspid area and along left sternal margin; pulse dicrotic, slightly collapsing; at autopsy, acute ulcerative aortic endocarditis.

Case 11. At apex, first sound followed by a soft systolic murmur, second sound replaced by a diastolic murmur; murmurs heard over body of heart; at autopsy, acute ulcerative aortic endocarditis.

Case 13. Mitral endocarditis, pericarditis with effusion; at autopsy, fibrous myocarditis, cardiac hypertrophy and dilatation; chronic and acute mitral endocarditis; pericarditis with effusion.

Tabulating the valve lesions, the acute changes were distributed as follows:

| | |
|---|---|
| Aortic valve alone | 4 |
| Aortic and mitral | 1 |
| Aortic and tricuspid | 1 |
| Mitral alone | 2 |
| Tricuspid alone | 1 |

The aortic was involved in 70% of cases, the tricuspid in 40%, the mitral in 20%.

Ulcerative endocarditis occurred six times, the aortic valve being the only valve showing ulceration. In only one case of aortic endocarditis, namely the case involving the aortic, mitral, and tricuspid valves, was the aortic lesion not ulcerative.

Chronic changes were found in the heart in eight of these ten cases; two cases of ulcerative aortic endocarditis started in previously healthy hearts. The chronic changes involved the valves alone in one case; valves and myocardium in three cases; valve, pericardium, and myocardium in one case; myocardium alone in one case; pericardium in one case; myocardium and pericardium in one case. There were chronic changes in the valves in five out of the ten cases.

Chronic changes in other organs were found in all of the ten cases, including nephritis, arteriosclerosis, cirrhosis, etc.

The lesion in the lung was a lobar pneumonia in nine cases; a multiple lobular pneumonia in one. Organizing pneumonia occurred twice, infarction, abscess, and gangrene of lung each once.

In addition to the two cases starting as acute articular rheumatism, arthritis occurred in four of the nine cases starting as pneumonia, three of the four patients dying, one having also meningitis.

Only four of the fatal cases were designated septicæmias. Blood cultures were made in five of the thirteen cases, but proved positive in only two of the more recent cases.

Lumbar puncture gave pneumococci in the four meningitis cases in which it was tried.

In most of this series there was little or no interval between the pneumonia and the complicating endocarditis or meningitis. In one case endocarditis developed in six days, and meningitis thirteen days after the temperature had reached normal.

## References.

Horder and Scofield. A second case of pneumococcal endocarditis treated by antipneumococcus serum. Lancet, Lond., 1905, I, 1333.

Livingstone and Jubb. Pneumonia with infective endocarditis and meningitis. Lancet, Lond., 1905, I, 486.

Osler, Wm. Malignant endocarditis. Brit. M. J., 1885, I, 467; 522; 577.

Preble, Herbert. Pneumococcus endocarditis. Am. J. M. Sc., Phila. and N. Y. 1904, n. s., CXXVIII, 782-797.

Thacher, John S. Report of a case of pneumococcus sepsis. Am. J. M. Sc., Phila. and N. Y., 1905, n. s., CXXX, 779-784.

Thorel, Ch. Endokarditis bei Pneumonie. Lubarsch Ostertag, Ergebnisse der Allgm. Path., usw., 1903, IX.

# ACUTE PERICARDITIS COMPLICATING ACUTE LOBAR PNEUMONIA.[1]

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During the period of sixteen years, viz., from May 15, 1889, to May 15, 1905, 658 patients suffering from acute lobar pneumonia have been admitted to the Johns Hopkins Hospital. These figures include all cases, both those admitted with the disease and those developing terminal pneumonias.

Acute pericarditis was present in 35[2] patients, or 5.31%. In 16, or 45.7%, pericarditis was recognized during life; in the remaining 19 patients it was only recognized at autopsy. Autopsies made in 27 instances confirmed the diagnosis of acute pericarditis or showed its presence when not suspected before death. The analysis of the cases is as follows:

*Age.*—The average age of the patients was 33 years. The complication occurs more frequently in young adults, only 7 patients out of the last 21 in this series being above the average age (33 years) and the majority were much younger.

*Sex.*—There were 24 males and 11 females. Of the males 11 were white and 13 colored; among the females 6 were white and 5 were colored.

*Duration.*—The duration of the illness being so indefinite and in many cases unobtainable, I have merely considered the time the patient was in the hospital, which in most instances was quite short. In 2 patients, however, it was long, due to a protracted illness of another nature (arthritis deformans and typhoid fever); in a third

[1] Read before the Johns Hopkins Hospital Medical Society, June 5, 1905.

[2] Since publishing this paper and while collecting the general pneumonia statistics, four (4) cases of pericarditis have been found in the hospital records and analyzed. The results of this analysis have been inserted in the different parts of the statistics when necessary. The main point to be noted in the change, is the reduction of our mortality from 93.5% to 88.5%.—J. A. C.

patient the development of an empyema caused much prolongation of the disease. The remaining 28 patients showed an average duration of 6 days.

*Lung Involvement.*—The portions of the lungs involved during the disease were as follows:

| Right side. | Times. | Left side. | Times. |
|---|---|---|---|
| Upper lobe | 2 | Upper lobe | 0 |
| Lower lobe | 1 | Lower lobe | 2 |
| Upper and middle lobes | 2 | | |
| Upper and lower lobes | 2 | | |
| Middle and lower lobes | 1 | | |
| All lobes | 5 | Both lobes | 3 |
| Total | 13 | Total | 5 |

The lungs on both sides of the chest were involved at the same time in 17 patients, the distribution of consolidation being as follows:

| | Times. |
|---|---|
| Right lower lobe and left lower lobe | 4 |
| All right lobes and left lower lobe | 3 |
| Right lower and left upper and lower lobe | 2 |
| Right lower and middle and left upper lobe | 1 |
| Right lower and middle and left lower lobe | 2 |
| Right upper and lower and left lower lobe | 1 |
| Right upper and lower and left upper and lower lobe | 1 |
| Right upper and left lower lobe | 1 |
| Right upper and left upper and lower lobe | 1 |
| Right upper and middle and left upper lobe | 1 |
| Total | 17 |

*Heart Condition.*—In regard to the recognition of the pericarditis during life it may be said that in 13 instances there was no note of any pericardial rub, or other symptoms to indicate a pericarditis. In 16 patients pericarditis was diagnosed. Five cases were doubtful; in one the patient was too restless and delirious for a satisfactory examination. Of the remaining four, the sounds in the lungs were so loud, that the heart condition was masked, though in one instance a suspicious rub was heard over the heart, but it was not sufficiently plain to justify a diagnosis of pericarditis. In the sixth doubtful case there was no note of any pericardial rub, but the increase of cardiac dullness to the right of the sternum was suggestive of an effusion into the pericardium and the autopsy in this case showed some excess of fluid.

*Complications.*—In the clinical histories pleurisy was by far the most common complication, occurring as follows:

Acute fibrinous pleurisy, right side, 8 cases; left side, 7 cases; both sides, 4 cases; pleurisy with effusion, right side, 1 case; left side, 1 case. The other complications were empyema 3 times; acute nephritis, acute endocarditis, parotitis, and pneumothorax once each. Of the associated diseases, typhoid fever, arthritis deformans, and acute articular rheumatism occurred once each, the pneumonia having developed during their course.

*Mortality.*—The mortality was extremely high, 31 patients out of the 35 dying, or about 88.5%.

*Remarks.*—A marked history of alcoholism was given by 10 patients. Occupation had little bearing on the disease, the majority being laborers as in most hospital series. Two patients gave a history of previous attacks of pneumonia. Another had had both pneumonia and acute rheumatic fever previously and one other acute rheumatic fever only. Two patients showed a general pneumococcus infection, the organism being cultivated from the blood during life. Four cases were admitted in active delirium and two became delirious during the course of the disease—delirium therefore occurring in 19.3%. There were two instances of terminal pneumonia or 6.45%. This small percentage is rather interesting as we know what a fatal complication pericarditis is and how often it is a feature of terminal infections in other cases. It does not seem so common in terminal pneumonia, judging from the small number of cases found here.

*The Autopsy Records.*—As so many of the fatal cases come to autopsy, their pathological and bacteriological findings should be reviewed, especially, because in many, no definite diagnosis could be made before death. During the past sixteen years 185 autopsies have been made at the hospital on cases of acute lobar pneumonia; among these there were 30 cases, or 16% with acute pericarditis, 27 of which are noted above, the other three having no clinical histories.

*Lung Involvement.*—In analysing these cases we find the lung involved as follows, according to lobes consolidated:

| Right side. | Times. | Left side. | Times. |
|---|---|---|---|
| Right upper | 2 | Left upper | 0 |
| Right lower | 1 | Left lower | 2 |
| Right upper and lower | 1 | | |
| Right upper and middle | 2 | | |
| Right lower and middle | 1 | | |
| All lobes | 7 | Both lobes | 2 |
| Total | 14 | Total | 4 |

In combination both sides of the chest were involved together in 12 cases as follows:

| | Times. |
|---|---|
| Right upper and left lower | 2 |
| Right upper and both left lobes | 2 |
| All right lobes and left lower | 2 |
| All right lobes and both left lobes | 1 |
| Right middle and lower and left lower | 1 |
| Right middle and lower and left upper | 1 |
| Right upper and lower and left upper and lower | 1 |
| Right lower and left lower | 1 |
| Right upper and middle and left upper lobe | 1 |
| Total | 12 |

*Pericarditis.*—The varieties of pericarditis were as follows in order of frequency.

| | Times. |
|---|---|
| Acute fibrinopurulent pericarditis | 10 |
| Acute serofibrinous pericarditis | 10 |
| Acute fibrinous pericarditis | 8 |
| Acute purulent pericarditis | 2 |

In 3 instances only, was a very large amount of fluid present. In two patients, one with 500 cc. and the other with 800 cc. of fluid, the clinical history was not obtainable, so the question as to whether the pericardial effusion was diagnosed before death cannot be answered. The third patient had 1000 cc. of fluid, but the associated empyema on the left side interfered with the recognition of the pericardial effusion and it was only discovered at autopsy.

*Bacteriology.*—In regard to the organisms cultivated and recognized, the presence of the pneumococcus only, when found, is tabulated, thus:

*Lungs.*—The pneumococcus was obtained in culture in 16 instances and found microscopically in cover-slip smears made at autopsy 7 times when the cultures were negative, a total of 23 in 29 autopsies. From the *pericardium* the pneumococcus was cultivated 12 times and the smears showed its presence in 7 other cases. Consequently, in 19 of the 29 cases of pericarditis the pneumococcus was the organism present. No other important organisms were cultivated, in most instances the cultures or smears being sterile or contaminated.

Bacteriological findings elsewhere in the body were as follows:

| | Times. |
|---|---|
| Pneumococcus cultivated from heart's blood | 5 |
| " " " pleural exudate | 3 |
| " " " empyema | 2 |
| " " " lung abscess | 2 |
| " " " mitral valve | 1 |
| " " " brain | 1 |

*Complications.*—Pleurisy was so frequent as to be regarded as more than a complication, being present in 29 of the 30 autopsies. The sides involved were as follows: right side, 13 times alone; left side, 8 times alone; both sides at same time in 7 instances. Pleurisy with effusion occurred 12 times. Empyema was found 3 times, twice on the right side, both of them being encapsulated between the diaphragm and lungs. In the third case the empyema was on the left side, not encapsulated. Abscess of the lung occurred twice and acute purulent meningitis and acute mitral endocarditis once each. Acute mediastinitis was present in a number of cases, its frequency being hard to determine exactly, as often no note of its presence or absence was given in the records.

*Remarks.*—In looking over both the clinical and pathological records, one is especially struck with the seriousness of pericarditis in acute lobar pneumonia. It is hard to say whether the cases of pneumonia, in which pericarditis occurred, were any more severe than usual or whether pericarditis is only one of the many manifestations which develop at the end of a severe pneumonia. A striking fact in the records is the more frequent involvement of the lung and pleura on the right side. This would seem to indicate that pericarditis is due to a metastatic process, through the blood or lymphatics rather than by direct extension from the lung or pleura. This is of interest in the light of the fact that great stress has been laid by many in previous reports on the synchronous involvement of the left lung and pleura, which as we know envelops the heart more than on the right side.

In the autopsy records, I found a case of a woman who had a large hemorrhagic infarct in the upper right lobe of her lung, the pleural surfaces over this area showing fresh fibrinous adhesions; a fresh serofibrinous pericarditis was also present. The lung and pleura were otherwise not involved, yet the cultures from the infarct and pericardium showed the presence of the pneumococcus. This case seems

strongly to favor the view of an infection by the blood stream or lymphatics rather than by direct extension.

Recent work also shows how often the pneumococcus can be cultivated from the circulation, or other pneumococcic processes outside of the lung involved. The great frequency of pleurisy may be of some importance in explaining the extension of the disease, but granting this, the right side has been found involved more than the left, the pleural surface of which (*i. e., left*) is much more in contact with the pericardium.

The prognosis of pericarditis complicating acute pneumonia, to judge from our own cases and the general statistics in the literature, is exceedingly grave. Our two cases of recovery were of interest, owing to the fact that both were associated with another disease; one, a white male, age 43 years, who was admitted for treatment of arthritis deformans and spondylitis, was in the hospital 237 days. After admission he had pneumonia involving the right and left lower lobes lasting several weeks; during its course a definite pericardial rub was heard for several days. There was no active arthritis at any time to suggest a rheumatic pericarditis; later the patient left the hospital much improved. The other instance of recovery was a white female, age 29 years, who was admitted with all the signs of pneumonia, with involvement of the right upper and lower and left lower lobes. A pericardial rub was present on admission and lasted several days. Later the patient had an attack of typhoid fever, with positive Widal reaction, rose spots, and an enlarged spleen; after remaining in the hospital 119 days she was discharged quite well.

The treatment of patients in whom the pericardial rub was recognized during life, was of the general supportive character, usually employed in pericarditis. Locally ice-bags and blistering were tried. All treatment except in the cases of two who recovered seemed to be unavailing.

In no instances was aspiration or free drainage tried.

*Literature.*—Upon a review of the literature bearing on pericarditis as a complication of pneumonia, opinions are found to vary somewhat as regards its frequency, mode of infection, and mortality. Most writers, however, agree as to its seriousness, thus:

Fowler and Godlee (1) found pericarditis 17 times in 128 fatal cases of pneumonia or 13.2%. They say: "It is generally stated that this complication (pericarditis) is more frequent in cases of

pneumonia in which a portion of the left lung in contact with the pericardium is consolidated, but in these fatal cases the right lung was involved 10 times, the left 6, and both lungs once."

Our statistics seem to agree closely with theirs.

Pye-Smith (2) says: "Pericarditis is not infrequent and is an extremely dangerous complication. Double pneumonia with pericarditis is almost invariably fatal. . . . . "Pericarditis follows more particularly when the pneumonia or pleurisy is on the left side. In 434 cases of pneumonia, pericarditis was present in 14, all fatal."

A. H. Smith (3) says: "This complication (pericarditis) occurs in 2 to 8% of the cases of pneumonia, according to different authorities. At the Presbyterian Hospital, N. Y., it was made out during life in 6 out of 485 cases of pneumonia, about 1.2%."

Strümpell (4) in speaking of the complications of pneumonia, after mentioning pleurisy, says: "Still worse is a sero-fibrinous or purulent pericarditis, which in not very rare instances, is revealed at autopsy as the special cause of death. We must note, however, that recovery sometimes takes place in spite of an empyema or a purulent pericarditis."

Osler (5) found pericarditis present in 5 of his 100 autopsies.

In their book on Pneumonia, Sturges and Coupland (6) say: "Pericarditis is an interesting and serious complication and in many instances its presence is not declared during life. It is mostly described as more common in association with pneumonia and pleurisy of the left side (this statement made on the authority of Bouillard) and hence may be regarded as due to a direct extension of the inflammatory process to the pericardium. But in an analysis of 144 autopsies (Middlesex Hospital, 1873-1889) this is by no means the rule, for out of 24 cases of acute pericarditis, in no fewer than 11 was the right lung involved, in 10 the left and in 3 both lungs. It may be remembered, however, that pericarditis was more frequently combined with pleurisy of the left side."

"In 23 cases of pericarditis and pneumonia coexisting, the right lung was consolidated in 16 either solely, which was the rule or with very slight consolidation of the left; of the remaining 7 cases, 4 were not distinctive." Among some statistics they quote are the following: "Leudet met 6 cases of pericarditis out of 83 pneumonias. Austin Flint 8 out of 133 cases. Behier 3 out of 114 cases of pneumonia.

Huss in his 2616 cases of pneumonia gives 22 cases of pericarditis, 12 of which were fatal."

Babcock (7) says: "Acute lobar pneumonia should certainly be given a place only subordinate to acute articular rheumatism, in the etiology of pericarditis." He quotes Preble as having found pericarditis in 92.4% of 79 fatal cases of pneumonia collected from the post-mortem records of the Cook County Hospital, Chicago. Preble came to the conclusion that the danger of pericarditis bears a distinct relation to the extent of lung involvement and is also more frequent in left than right-sided pneumonias.

McCrae, Fyshe, and Ainley (8) in an analysis of 486 cases of pneumonia and 100 autopsies, found pericarditis in 11 cases, about 2.3% (ours 5.26%), whereas the analysis of the autopsies gave a percentage of 17% (ours 16.2%). "The discrepancy that exists between the clinical and pathological records is easily understood when one remembers the comparatively short time in which a pericardial friction rub may be present and the small amount of fluid present in many cases." "Of their cases 7 occurred with involvement of both lungs, 5 of the right side and 4 of the left."

Anders (9) found acute pericarditis 14 times in 275 cases of pneumonia, about 5%, and Geo. W. Norris (10) in 500 cases of pneumonia in the Pennsylvania Hospital (1897-1901), found acute pericarditis as a complication in 4 cases, 3 of which were fatal.

J. A. Scott (11) reports and discusses an interesting case of purulent pericarditis secondary to pneumonia with operation and recovery. In cases where fluid is suspected, free drainage even in desperate cases may give favorable results at times. One of our cases which might have yielded better results with aspiration and free drainage, was the one mentioned with a large pericardial effusion (1000 cc.), but the accompanying left-sided empyema masked the pericardial condition.

John B. Roberts (12) has an interesting article in the American Journal of Medical Sciences for December, 1897, on the surgical treatment of the suppurative pericarditis; and Morris Manges (13) says: "There have been 6 cases of pericarditis in the Mt. Sinai Hospital, N. Y., 3 recovered and 3 died. Aspiration did good in all but one case." He reports at length the history of a boy with double pneumonia and purulent pericarditis, who recovered in 38 days after aspirating, opening, and drainage of the pericardium. "Skoda's two rules for entering the pericardial sac are given: (1) Distension with a

large exudate, showing no tendency to absorption and the patient getting worse, and (2) a vital indication is intense dyspnea."

Among the French are found the following statistics:

Netter (14) says: "Lesions of the pericardium are not at all exceptional; they are analogous to those of the pleura with which they often coexist."

"It varies with the different years and the severity of the pneumonia, thus we note its frequency in 1804-05, again in 1837, '76, '82, '86, and 1890." In our series pericarditis was most common in 1900, there being six cases. As to statistics, Netter says: "Ormerod found pericarditis 12 times in 100 pneumonias, Leudet 6 in 83 cases, and Grissole 3 times in 58 cases of pneumonia."

Vignau (15) collecting and combining various statistics, believes that it occurs in from 5 to 8%.

Landouzy (16) says: "Pericarditis was observed in 8% of Netter's cases. Rarely is it accompanied by an abundant effusion and coexists often with other pneumococcic manifestations as meningitis, endocarditis, etc." P. Merklen (17) says: "Bouillard considers the complication (pericarditis) as common, others only in 1 to 2% of cases."

Among the German statistics, Sello (18) reports upon 750 cases of pneumonia, in which he found pericarditis in 7 cases, or about 0.9%; 5 died and 2 recovered. In 4 purulent cases, the right lung was involved in 3 and the left only once. Sello reports other men as finding this complication as follows; von Jürgensen in 0.5%, Fismer in 3.9%, and Rychner in 2.7%.

To illustrate the more frequent involvement of the right lung John L. Steven (19) found pericarditis 13 times in 120 fatal cases of pneumonia; the right lung being involved in 8 cases, the left in 3 cases and both lungs in 2 cases.

John Hay (20) reports in the Lancet on 200 cases of acute lobar pneumonia. He found 9 cases of pericarditis, 6 of which were fatal; he says: "I found it to be a most serious complication, probably because it is so potent in damaging the myocardium, also from the fact that it is sometimes merely a terminal event in a severe case or again it may be and I believe, is, frequently, a symptom of its severity."

In a report of 28 cases of suppurative pericarditis in children, George F. Stille (21) found that 11 gave positive cultures of pneumococci; of the rest, although no bacteriological examination was made of the pericardial fluid, yet the other associated lesions, empyema or pleurisy following a pneumonia, yielded pneumococci.

Sears and Larrabee's report (22) of 949 cases of pneumonia I wish to give somewhat in detail because our observations seem to agree fairly closely with theirs. "The recognized difficulty of diagnosing pericarditis in the presence of pneumonia received a further illustration in these cases, since only about half were discovered during life, and in some of these, which were represented only by a friction rub, the inflammation may have been outside and not within the pericardial sac, yet the number that was found at autopsy, shows that it is not a very rare complication, at least among the fatal cases, since it was found in 8 of 72 autopsies. Out of 19 cases in which it was diagnosed, 11 died; in some of which it was simply an incident in a general pneumococcus septicemia. In 5 only a considerable amount of fluid was present and in 3 was there sufficient to have embarrassed the heart."

"It occurred more frequently when the right lung alone was attacked, for in 10 of 18 cases in which there were complete data, it was confided to that side. The distribution of lung involved being as follows: Right upper, 3 cases; right lower, 2 cases; whole right lung, 3 cases; left upper lobe, 1 case; left lower, 1 case; whole left lung, 1 case. The following combinations of both lungs occurred *once*, each whole left lung, with right lower; whole left lung, right middle; whole right lung, with left lower; right upper and lower and left lower; right middle and lower and left lower; right upper and middle, and left lower; and right and left lower once. Acute mediastinitis was found 3 times at autopsy."

Finally F. P. Henry (23) reports upon the clinical and pathological findings in a case of pneumonia of the left side with purulent pericarditis and says: "A study of this case has convinced me that the diagnosis of pericardial effusion complicating left-sided pneumonia, is to be made, as much by the symptom (cyanosis, rapid pulse and dyspnea), as by the physical signs."

*Conclusion.*—It may be said that pericarditis developing during the course of an acute lobar pneumonia, is a most serious and important complication occurring more especially in young adults, frequently insidious, latent, and often not recognized during life.

It appears to arise as frequently by a metastatic process as by direct extension.

Treatment is very unsatisfactory and often unavailing, except when fluid is present in which case it is more surgical than medical.

In all patients with pneumonia, a most careful watch should be kept on the heart, as this complication appears to be much more frequent than is generally supposed, and urgent treatment in the early stages may materially reduce a high mortality.

Bibliography.

1. Fowler and Godlee. Diseases of the Lungs, p. 208.
2. Albutt's System of Medicine. Vol. VI, p. 119.
3. Twentieth Century Practice of Medicine. Vol. XVI, p. 65.
4. Strümpell. Text-Book of Medicine, p. 204.
5. Osler. Text-Book of Medicine, p. 124.
6. Sturges and Coupland. Pneumonia, p. 105.
7. Babcock. Diseases of the Heart, p. 46.
8. McCrae, Fyshe, and Ainley. American Med., Jan. 23, 1904.
9. Anders. American Med., May 9, 1903.
10. Geo. W. Norris. Am. J. M. Sc., Vol. 121, p. 684.
11. J. A. Scott. N. Y. Med. J., Jan. 30, 1904.
12. John B. Roberts. Am. J. M. Sc., Dec., 1897.
13. Morris Manges. Med. Record, Jan. 13, 1900.
14. Bouchard and Brissaud. Traité de Médicine, Vol. VI, p. 479.
15. Vignau. Thèse, Paris, 1895.
16. Brouardel. Traité de Médicine, Vol. VII, p. 418.
17. Brouardel. Traité de Médicine, Vol. VI, p. 89.
18. H. Sello. Zeit. f. Klin. Med. Bd., 36, p. 128.
19. John L. Steven. N. Y. Med. J., Aug. 10, 1901.
20. John Hay. Lancet, June 11, 1904.
21. George F. Stille. Brit. Med. J., Sept. 7, 1901.
22. Geo. E. Sears and R. C. Larrabee. St. Paul Med. J., Vol. IV, No. 7.
23. F. P. Henry. International Clinics, Vol. IV, 12th Series.

# EMPYEMA IN ACUTE LOBAR PNEUMONIA.

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This must be regarded as a possible complication in every patient with lobar pneumonia, and when one considers the almost invariable pleurisy when the process reaches the surface of the lung, the wonder is that empyema occurs so rarely. Peculiarities in the organism or in the individual resistance must have an important bearing on its development. The variation in the incidence from year to year suggests that the most common cause must be in some peculiarity in the organism. It is, of course, quite analogous to the varying occurrence in different years of certain complications as we see in typhoid fever. When one considers the possibility of infection of the pleura, for probably pneumococci are present there in every attack of pneumonia due to pneumococcus, the number of cases is not large. Thus Musser and Norris[1] found 2.2 per cent among 13,550 clinical cases, and 5.1 per cent in 973 autopsies. In the present series there were 29 cases among 805 of lobar pneumonia (3.6 per cent), in the medical service of the Johns Hopkins Hospital from May 15, 1899 to May 15, 1907. Sometimes one is inclined to think that it would be better if empyema occurred more frequently, as then perhaps it might be recognized more quickly. It is no rare thing in every large clinic to see patients brought in, who have had an unrecognized empyema for weeks and perhaps months. In these cases, even with the best results possible after the delay, the patient may be condemned to more or less serious permanent damage.

Taking empyema in general it is of interest to note what a comparatively small proportion of the total cases follow pneumonia. Lord[2] among a series of 252 cases of empyema found that 136 had followed lobar pneumonia. Hale White, in a study of empyema in Guy's

[1] Osler's Modern Medicine, Vol. II, p. 529.
[2] Osler's Modern Medicine, Vol. III, p. 833.

Hospital, London,[3] found that among 325 consecutive cases of empyema, 41 (12.6 per cent) occurred after a lobar pneumonia. This study from Guy's Hospital suggests that both the frequency and severity of empyema have increased. Thus from 1883 to 1890, among 445 cases of pneumonia there were 7 of empyema (1.5 per cent), and from 1891 to 1898 there were 196 cases of pneumonia with 38 of empyema (4.24 per cent). Hale White suggests that the prevalence of influenza may have an important bearing on the relative frequency of empyema. Apart from this, however, there are frequently "empyema years," when an unusually large number of cases develop.

The special features of the cases occurring in the Johns Hopkins Hospital are here studied and as the aim is to consider empyema occurring with lobar pneumonia, rather than empyema in general, the cases of empyema apart from lobar pneumonia are not included.

*Occurrence.*—This varies markedly from year to year and the incidence is rather curious. The figures for each year are:

| | |
|---|---|
| 1890.....2 | 1902.....2 |
| 1897.....2 | 1903.....2 |
| 1898.....1 | 1904.....3 |
| 1899.....1 | 1905.....6 |
| 1900.....7 | 1906.....1 |
| 1901.....1 | 1907.....1 |

It will be noted that duing the years of the great influenza epidemic, 1889 to 1892, there were very few cases, only two in 1890, and from this until 1897 not a single case occurred. This certainly does not suggest that the prevalence of influenza had any influence on the occurrence of empyema here. The number of cases in 1900 is striking. At this time the antipneumococcic serum was being used and one might be tempted to say that this had some influence. The almost equal number in 1905, when the serum was not used, disproves this view. The number of cases of pneumonia varies from year to year but both 1900 and 1901 were years with a large number of cases.

A co-existence in the incidence of empyema and pericarditis has been noted. This is rather marked in this series and for comparison the years of occurrence of cases of pericarditis are given. It is seen that in 1900 and 1905 the maximum number of cases of both complications occurred.

[3] Lancet, ii, 1900, p. 1331.

| | |
|---|---|
| 1890.....1 | 1899.....2 |
| 1892.....2 | 1900.....8 |
| 1893.....1 | 1901.....2 |
| 1894.....1 | 1902.....2 |
| 1895.....1 | 1903.....3 |
| 1896.....2 | 1904.....2 |
| 1897.....1 | 1905.....5 |
| 1898.....2 | 1906.....2 |

*Is Empyema a Complication or a Sequel of Lobar Pneumonia?*—Opinions as to this vary but the findings in this series suggest that in the great majority of cases it is a complication and is present before the termination of the pneumonia. This is supported by its recognition during the course of the original disease, as in three of this series. In one it was recognized by aspiration on the fifth day of the pneumonia; in two others dying from the pneumonia on the eighth and ninth days respectively, it was found at autopsy.

The history of one of these cases is as follows:

**Med. No. 8546. The patient, a white male, aged 36 years, was admitted on the seventh day of the disease with involvement of all the lobes on the right side. Vocal fremitus was well felt throughout the whole right back. On the ninth day there was evidence of consolidation in the lower left lobe and the right side showed signs of clearing, the tubular breathing being less intense and some rales being heard. Death occurred on the ninth day, and at autopsy consolidation of the whole right lung, with beginning consolidation of the lower lobe of the left lung, was found. The two layers of the pleura were adherent over the upper part of the right lung. Below there was about 500 cc. of purulent fluid. The pleura itself was œdematous and hæmorrhagic.**

Another point is the examination of the temperature charts. In 21 patients the temperature never became normal, the fever of the pneumonia being continuous with that of the empyema (Fig. 1); in 4 others it touched normal once but rose again (Fig. 2); in 2 it was normal for less than twenty-four hours, in one, for twenty-four hours and in one, for three days. The fact that in only one patient was there normal temperature for more than twenty-four hours, between the termination of the pneumonia fever and the beginning of that due to the empyema, supports the view that the empyema is usually present before the end of the pneumonia. That in some cases the empyema may be a sequel seems beyond doubt. In one patient who had a large abscess in the left pectoral region, opened on the sixty-

seventh day, and in which no connection with the pleura could be found, the temperature after removal of the pus fell to subnormal for nine days. After this fever returned and with it signs of fluid at the left base, which was found to be purulent nine days later.

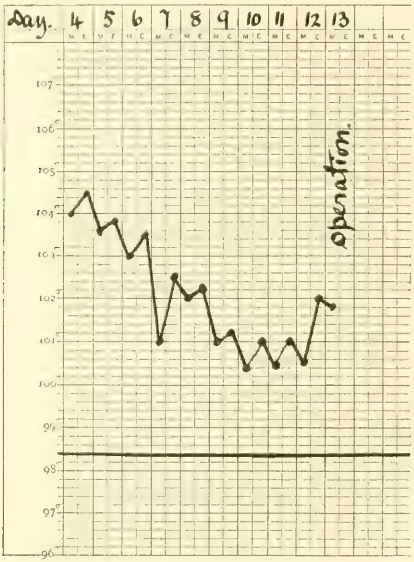


FIG. 1.—This shows a temperature curve which continued elevated The symptoms suggested a crisis on the seventh day.

*Etiology.*—The age incidence is as follows:

| | | |
|---|---|---|
| 1-10 | 6 | cases. |
| 11-20 | 4 | " |
| 21-30 | 12 | " |
| 31-40 | 6 | " |
| 41-50 | 1 | " |

The number below the age of ten is large when we remember that there are relatively few children admitted to the wards.

*Sex.*—There were 24 males and 5 females; the proportion in the whole pneumonia series being about 4 males to 1 female.

*Color.*—There were 19 white and 10 colored, a relatively larger number proportionately among the colored race. In the total admissions for pneumonia the colored show a relatively high percentage, the ratio being about 3 white to 2 colored. The proportion of white to colored in total medical admissions is about 5 to 1.

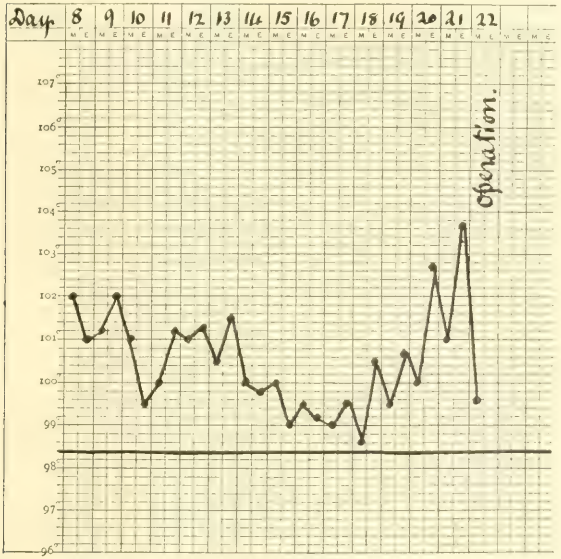


FIG. 2.—This shows a temperature curve reaching normal once and then rising at once.

*Contributing Causes.*—It is difficult to say that any condition occurring during an attack of pneumonia has any influence in the production of empyema. Pneumonia, which has followed trauma, particularly if there were fracture of a rib, might be regarded as a predisposing cause. In the study of this series it is not possible to assign any importance to anything in the family or previous history. Four patients gave a tuberculous family history and two had previous attacks of pneumonia.

*Organism.*—As regards the organism present, the pneumococcus is the most frequent. Among 46 cases quoted by Musser and Norris, pneumococci were found in 24, streptococci in 10, tubercle bacilli in one, while 11 were sterile. In the series reported by Sears and Larrabee,[4] it was found that all cases of pneumonia coming to autopsy showed pneumococci in the exudate, whether this was fibrinous, serous, or purulent. It has to be remembered that after a time the pneumococci may die and cultures be sterile. Sometimes pneumococci may be found in cover-slip preparations of the pus and yet the cultures are sterile. In the present series among 22 cases in which cultures were obtained during life, pneumococci were found in 20 and streptococci in 2.

*Character of the Attack of Pneumonia.*—It is difficult from a study of the histories to make any statement as to the influence of the severity of the attack of pneumonia. As a rule, however, one is given the impression that many of the attacks were severe. As to the amount of involvement an interesting point is that in only three cases was one lobe alone involved. In every instance of this series there was involvement of a lower lobe, and the empyema occurred after the involvement of the lower lobe on the affected side in every case. As to the number of lobes involved: there was one lobe in 3, two lobes in 16, three lobes in 8, and four lobes in 2. As to the number of times one side or the other was involved the figures are: right side 22 and left 18. The empyema was on the right side in 14, and on the left in 15 cases. There was no example of the empyema being on the side opposite to the pneumonia.

*Pathology.*—It is evident that the findings will vary greatly with the time at which death occurs. In a patient dying of the pneumonia and having empyema there is an entirely different condition from that met with in one dying months later from exhaustion and sepsis. The character of the process must also influence the changes, a general exudate will be accompanied by more changes than a sacculated one.

*Pleura.*—In the patient dying on the eighth day the pleura was dull and in many places was covered by thin fibrin. The cavity contained about 100 cc. of turbid fluid. In one dying on the ninth day the pleura showed a covering of a rather thick purulent exudate with fluid

[4] Medical and Surgical Reports of the Boston City Hospital, 1901, Vol. XII.

in the cavity. The pleura itself was œdematous and hæmorrhagic, the latter being especially marked on peeling off the exudate. This hæmorrhagic character was very marked in one patient dying on the fifteenth day. With every day the empyema exists the pleura tends to become thicker. This is as true of serous effusions and can be recognized in successive tappings. The thickening may develop rapidly, thus in one patient in whom the pleura was opened on the tenth day, death followed on the twenty-fourth day from streptococcus septicæmia. At autopsy the pleura was found to be markedly thickened. In another patient, who was drained on the twentieth day, death occurred from myocarditis on the forty-sixth day. At autopsy the incision was found to open into a small cavity from which two sinuses radiated. The pleura was everywhere adherent, and while above the adhesions could be broken down, below they were very firm. This variation in the degree of thickening is often very striking and, in an encapsulated empyema the thickening may be quite local. In later stages the amount of thickening may be so extreme that the pleura occupies a comparatively large part of that side of the thorax. There may be calcareous deposit, but these changes are of course not peculiar to the empyema with pneumonia.

*Lung.*—The same differences are found as in the pleura, depending on how long the pleuritis has continued. Thus in the cases examined early the lung was found to be consolidated and about of normal size. The time which is required for the development of fibroid change is interesting. The earliest in this series was found in a patient dying on the twenty-fourth day from the onset of the pneumonia. At autopsy there was marked collapse of the lung and decided fibroid change. The same patient showed marked thickening of the pleura. Pulmonary infarction was found in the lower lobe on the affected side in two instances.

*Effusion.*—The character of this varies greatly, also depending on the time of examination. In the cases coming to autopsy early it was thin and grayish; in the others in which an operation had been done there was comparatively little found, but what was there was thick and purulent. The same variation is seen in patients who are aspirated and some days allowed to elapse before another tapping or operation. The fluid usually becomes much more purulent in the interval. It must be remembered that the upper part of the fluid may be much thinner than that in the lower part of the pleural cavity.

*Mode of Onset.*—Is there any definite mode of onset in empyema? To determine this it is essential to know the *time* of onset and this is almost impossible to do. In fact by the physical signs it may be difficult to determine whether the onset is during the course or immediately after the termination of the pneumonia. To test the prevail-

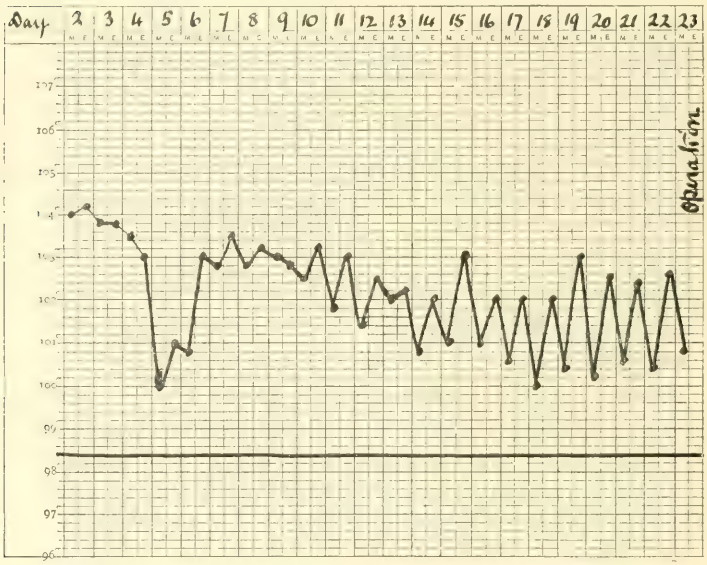


FIG. 3.—The drop in temperature on the fifth day was apparently a crisis. There was no extension of the pneumonic process after this.

ing opinion a number of physicians were asked whether they considered empyema a complication or sequel of pneumonia, and the replies were about equally divided.

As regards the onset in relation to the pneumonia, in 21 cases of this series it may be said that the temperature never became normal (Figs. 3 and 4); in 4 others it touched normal once but immediately rose again; in 2 it was normal for less than twenty-four hours; in 1,

normal for twenty-four hours, and in 1, normal for about three days (Fig. 5). One patient died a few hours after admission, from the pneumonia; empyema was found at autopsy. There were really no special features, such as a chill or onset of pain, which could be considered as marking the beginning of the empyema.

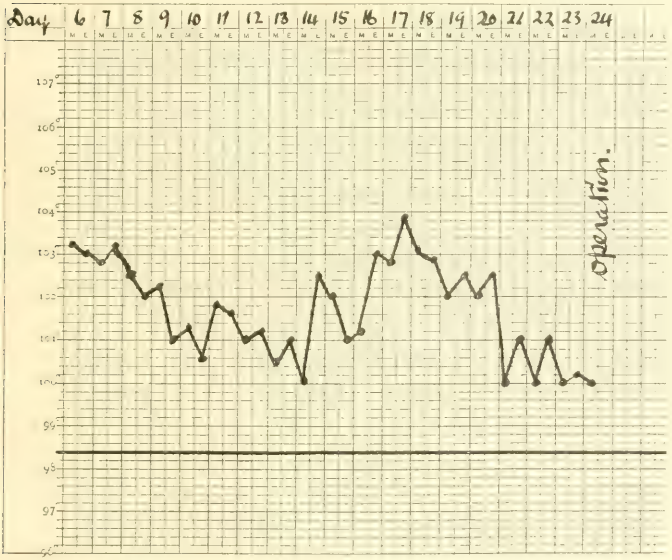


FIG. 4.—Showing a temperature curve which did not reach normal.

*Symptoms.*—The most constant one is the persistence of fever. The general condition may show very slight change or the patient may emaciate rapidly, lose color and show a sallow, unhealthy appearance. In some patients after the termination of the pneumonia there is decided improvement for some days and then the general condition becomes worse. The amount of discomfort varies greatly, some patients being perfectly comfortable, while others suffer greatly from distress and dyspnœa, occasionally pain. In a few patients the distress

became very acute in a short time. An example is seen in the following:

Med. No. 18,234. A male, aged 24, was admitted on the second day with involvement of the middle and lower right lobes. The termination was by crisis and the temperature fell to 99° on the ninth day, but rose again at once. The signs in the right side persisted, there being dulness, tubular

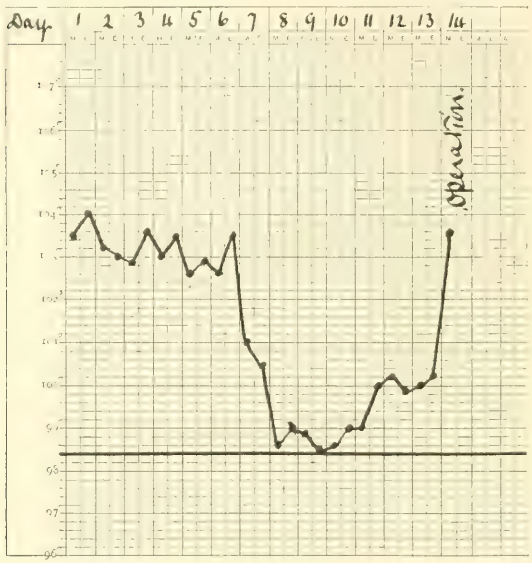


FIG. 5.—One of the few instances in which the temperature fell to normal; this, however, was only for a short time.

breathing and many rales over the lower right back. On the thirteenth day the temperature fell to 99° for a few hours. Immediately after this the patient's condition changed markedly, he had extreme distress and very severe pain in the right side. The pulse rate was somewhat increased but was not very rapid. The respiratory rate was high, usually being over sixty. On the fifteenth day there was flatness over the lower right back, but the breath sounds were fairly well heard down to the base. A needle was put in the lower right axilla and again in the back but only

a few drops of blood were obtained. On the following day it was noted that the breath sounds had suddenly become suppressed. The leucocytes rose from 30,000 to 53,000. Punctures were again made in three places, and at the angle of the scapula, purulent fluid was obtained which contained streptococci. Operation was done at once, the eighth rib was resected and a considerable quantity of pus obtained. The patient made a good recovery.

It is possible, as is suggested by the rapid change in the physical sign, that the effusion may have increased very rapidly and so have caused the marked distress. A similar picture is sometimes seen in the instances of rapidly increasing serous effusion.

In a few patients there was constant severe pain in the affected side. Should the condition go for some time without being recognized, chills and sweating may appear. The earliest occurrence of a chill was on the twentieth day, and of profuse sweating on the eighteenth day.

*Fever.*—It is difficult to give any definite classification of the forms of temperature curve. As already stated, the temperature usually continued elevated after the termination of the pneumonia. The most common curve showed considerable irregularity, varying from 99° or 99.5° to 102° or 103°. In some instances the fever was high and persistent. In only two might it be said to be slight. Among the unusual curves was that seen in a patient whose temperature did not fall after the pneumonia, but gradually declined until the twenty-second day when pus was obtained. In another patient pus was found on the sixteenth day and the temperature from the thirteenth to the fifteenth day was almost normal. There is no rule which can be laid down as to the fever curve. It does not necessarily become higher with the persistence of the empyema.

*Pulse.*—This showed some variation but the most frequent course was that it remained rapid throughout the pneumonia and then subsequently during the empyema. This occurred in 14 cases. In 4 it fell practically to normal at the termination of the pneumonia and then rose gradually. In 2 it stayed at about 100 throughout. In 3 it was rapid during the pneumonia and then fell practically to normal during the empyema. In 2 it did not show any special increase at any time.

*Respiration Rate.*—This showed more constant change than the pulse rate. In 23 the rate was rapid throughout, never reaching normal after the termination of the pneumonia. In 6 of these the rate with

the empyema was not very high, 32 being the usual maximum. In 3 the respiration fell practically to normal after the pneumonia and did not show any special increase. To some extent there was a tendency for the increased pulse and respiration rates to occur in the same patient. In a few, high fever occurred with rapid pulse and respiration rate.

*Leucocytes.*—These showed considerable variation. In 11 they were higher with the empyema than during the pneumonia, and in 3 showed no special change. In almost all the patients there was a marked leucocytosis, the lowest count being 10,000 in a patient who died on the ninth day of the pneumonia. The leucocytes were not over 15,000 in one; varied from 10,000 to 20,000 in 7; from 20,000 to 30,000 in 16; from 30,000 to 40,000 in 2; reached 50,000 in 1; and varied from 23,000 to 63,000 in 1. The last figure was the highest one reached in the series. On the whole it may be said that the leucocyte count did not prove of material assistance in the early recognition of empyema.

*Physical Signs.*—In considering these it must be kept in mind that empyema secondary to pneumonia is a different thing from a primary empyema. How much the presence of consolidated or clearing lung influences the physical signs is hard to state, but it seems probable that it must do so in some instances and it is likely that this varies greatly, depending on the degree of consolidation, amount of lung involved, rapidity of resolution and the quantity of exudate. This applies especially to the physical signs early in the course of empyema.

The special importance of the study of the physical signs is in regard to early diagnosis, for to this all our energies should be directed. It is evident that as regards inspection we may have no great difference in the findings in empyema and in pneumonia. The same is true to some extent of percussion and it is therefore to palpation and auscultation that we must turn for the greatest aid.

*Inspection.*—The study of the records does not suggest that this was of great aid in diagnosis. Of course there was restriction of movement, but as a rule this did not differ from that seen during the pneumonia. In a few instances the movements decreased after the acute period of the pneumonia was over, and in others it was noted that the intercostal spaces were more bulging. Increased bulging of the whole side was occasionally noted toward the end of the third week. Displacement of the heart to any extent was not noted in a single patient.

*Palpation.*—This would seem at first thought to be of the greatest importance, for do we not make it often the deciding point in the diagnosis between consolidation and pleural exudate—the results of aspiration being excluded. The records as to this show that in 10 cases the vocal fremitus was *distinctly present although diminished.* In reference to this point the age of the patients is of interest. Physical signs are often so unusual in children that one might expect a large proportion of these instances of retained vocal fremitus to have been in young patients. But the contrary is the case and only one was below the age of fifteen years, which is a relatively low proportion. It may be said that so far as could be made out at operation, in only one of these cases was the empyema encapsulated. In 3 others, in addition to the 10 with retained vocal fremitus, the note reads that vocal fremitus was diminished, which probably means that it was still present though this is not expressly stated. These notes were made by Prof. Osler, Dr. Thayer, Dr. Futcher, or the writer. In 2 cases it was noted that with wooden dulness the vocal fremitus was still present. In one patient it was present on the fifteenth day and entirely gone on the seventeenth.

As to the explanation of this phenomenon it is probable that the degree of tension has much to do with it, as suggested by Calvert[5] in commenting on an instance of massive effusion with retention of the vocal fremitus. It seems probable that with a consolidated lung, which can not retract and which itself transmits the vocal fremitus more strongly than normal, and fluid in addition, conditions are present which permit the transmission of vibrations. It is of interest that in a number of cases at operation it was noted that the lower surface of the lung was adherent to the diaphragm.

One other point noted on palpation was definite local tenderness. This was found in one patient. There is a certain sense of resistance which is suggestive of fluid, usually made out better on percussion than by palpation alone. Still it can sometimes be made out on ordinary palpation.

*Percussion.*—This, of course, may show but little change from the dulness noted during the pneumonia. The most marked changes were, (a) a gradual change in the character of the note, which became duller and sometimes acquired a wooden quality, usually very characteristic; and (b) some clearing of the note at the end of the pneumonia

[5] Jour. of the Amer. Med. Assoc. 1907, XLIX. p. 1921.

which was followed by increasing dulness. Of the cases in which the records are satisfactory, there were 11 in which the dulness increased, the change being generally described as from dulness to flatness. In 5 the note was dull throughout without any special change, and in 3 it was flat throughout. Distinct movable dulness was obtained only in one case.

*Auscultation.*—As a rule marked changes in the breath sounds were made out. In 5 no breath sounds could be heard on ordinary breathing. In 22 they were diminished, 5 had a very distant tubular breathing, 4 had feeble breathing which was not tubular, and 1 had quite nasal sounds. In 4 instances the feeble breath sounds were accompanied by rales, which were described as faint in 2 and as coarse in 2. In some instances the suppression of the breath sounds was very marked and the change in the breath sounds on shifting the stethoscope a short distance was suggestive. The change in the voice sound was frequently marked, a very definite nasal quality being often noted. This curious quality in the voice sounds was a great aid in diagnosis, and on auscultation was of more value than the character of the breath sounds. The quality is a difficult one to describe in words, perhaps it comes closest to an accurate description by being termed nasal. It is a quality which has to be heard to be appreciated. In some instances the change to this was very sharply marked from more normal sounds, heard perhaps an inch above.

*Time of Recognition.*—Taking the time from the onset of the pneumonia, this was during the first week in 1, the second week in 7, third week in 10, fourth week in 4, fifth week in 2, sixth week in 1 and thirteenth week in 1. The first, recognized during the first week, was the instance in which the condition cleared with aspiration, and in the last, found on the eighty-seventh day, the empyema apparently was a late development.

*Complications.*—(a) Connected with the lung. *Perforation into a bronchus* occurred in one case. Netter's estimate that this occurs in about one quarter of the cases would seem much too high. Of course, the time at which operation is done will have an important influence. Perforation of a bronchus rarely occurs until the third or fourth week and is not likely to happen after operation. In the one instance here, operation was done after the perforation and the patient made a good recovery. Five years later it was found that there was very little difference in the two sides of the thorax.

*Pulmonary tuberculosis* may co-exist, as in one instance in the series in a patient who apparently had pulmonary tuberculosis in addition to the lobar pneumonia. Tubercle bacilli were found in the sputum and, with the persistence of physical signs, suggested that the diagnosis of lobar pneumonia was wrong and that the condition was entirely tuberculous. However, aspiration showed empyema; pneumococci were obtained from the fluid. He made an excellent recovery.

*Abscess of the Lung.*—This occurred in one instance and is of interest, as apparently it occurred with the empyema but quite distinct from it. The history is as follows:

Med. No. 18,212. The patient, a white female, aged 28 years, was admitted with involvement of the right and left lower lobes. On the twelfth day it was noted that the dulness at the left base had increased, with wooden resistance and marked tenderness on percussion. The vocal fremitus and breath sounds were diminished but not absent. A needle was put in at the angle of the left scapula and pus obtained. This had a very foul odor and was rather thick. Operation was performed the same day, the eighth rib being resected in the axillary line. A limited cavity, about 8 cm. in diameter was found, which was definitely walled off and was regarded as an encapsulated empyema. It contained thin purulent material, quite unlike that obtained previously by puncture a short distance away. A second aspiration, 6 cm. nearer the spine than the encapsulated area, yielded gray, foul pus. The rib was resected over this and a small cavity found, walled off at the sides, and with the inner part formed of lung tissue. Here, too, the lung was firmly bound to the chest wall all about. The two areas were quite separate from each other. The patient made a good recovery and was discharged on the twenty-ninth day after operation.

*Cardiac Complications.*—These may be present as a complication of the attack of pneumonia or result from the empyema. In many cases it may be difficult to say which is the case. *Pericarditis* occurred in two instances; both patients died. In one the pericarditis was present during the pneumonia. Operation was done on the fifteenth day, the patient's condition always having been desperate. Death occurred on the twenty-fourth day, the heart having been very rapid throughout. In the second case the patient was admitted on the tenth day, after having been in a stable without any attention for several days. He died on the fifteenth day and at autopsy purulent pericarditis and a small amount of fluid in one pleural cavity were found.

*Endocarditis.*—This occurred in one instance. The temperature fell to normal on the eleventh day and became elevated again on the fifteenth day. Operation was done on the seventeenth day and a small encapsulated cavity found between the lower left lobe and the diaphragm. On account of the physical signs aspiration was done nearer the spine than the operation wound and a second collection of pus obtained. The two collections of pus were distinct from each other. After this the patient did badly, the heart became more rapid and death occurred on the fortieth day. At autopsy endocarditis of the tricuspid valve was found. In this case it seemed probable that the endocarditis developed after the empyema, although, of course, there can be no certainty as to this.

*Myocarditis.*—Slight grades of this are probably common. As a serious factor it figured only in one case. Operation was done on the twentieth day. It was noted that during the pneumonia and before operation, the pulse was persistently rapid. After operation the patient did badly although the state of the wound was satisfactory. The temperature fell but the pulse continued rapid. The patient lost ground and after pulmonary infarction death soon occurred. At autopsy marked myocarditis was found.

*Sequelæ.*—The commonest sequela is some degree of permanent change in the side affected, which may vary widely in extent. In many only a slight shrinking, in others there may be extreme deformity. With this there may be scoliosis and marked displacement of the heart. Bronchiectasis and fibroid changes in the lung may occur. Recurrence of the empyema does sometimes happen but there was no instance in this series such as that recently reported by Pryor.[6] There was one instance of suppuration in the site of the scar one year later. The empyema was operated upon on the sixteenth day; the patient made a good recovery and was discharged five weeks later in excellent condition. One year later she returned with a history of having been well until ten days before, when she had fever and slight chills. A week later she noted tenderness in the scar, and about its centre a red tender area was found. This was incised and pus found, but the cavity did not seem to communicate with the pleura. The wound healed in ten days.

*Fatal Cases.*—Seven of the patients died, a percentage of 24.1. A study of these is interesting. Two died of the pneumonia, one on the

[6] New York Med. Jour. Vol. 86. 1907, p. 1165.

eighth and the other on the ninth day. In one patient, admitted practically moribund, fluid at one base was diagnosed from the physical signs, but it was small in amount and did not seem to demand operation as the patient was dying from the pneumonia. In the other the empyema was not recognized during life.

Of the others one was a child aged 3 years, in whom the empyema was recognized on the ninth day, aspiration was done the next day and, as no improvement followed, operation was performed. Streptococci were found and death followed on the twenty-fourth day, apparently from streptococcus septicæmia. All the remaining three had some complication. In one, the empyema was recognized on the twelfth day while the pneumonia was still extending; operation was done on the fifteenth day. Pericarditis appeared and the patient died on the twenty-fourth day. In another, admitted on the tenth day, the condition was desperate. The patient had been lying in a stable with no care. Death occurred on the fifteenth day, pericarditis and meningitis having appeared. Empyema was found at autopsy. In another case, the empyema was recognized on the seventeenth day and operation was done. He died on the fortieth day with endocarditis and meningitis. In the remaining case operation was done on the twentieth day. The patient did not do well although the condition of the wound was satisfactory. There was evidently myocarditis and the patient died on the forty-sixth day, apparently with infarction of the lung.

*Prognosis.*—Judging from the experience of this hospital, the death rate in empyema is about the same as that in pneumonia. In some patients, dying from the pneumonia itself with empyema present, the complication probably has little influence on the fatal result. With a streptococcus empyema and septicæmia, the empyema must probably be regarded as contributing largely to the outcome. In this series complications were important and when pericarditis, endocarditis or meningitis appear as complications of empyema, the question must always arise as to whether earlier recognition and operation might not have diminished the chance of the subsequent conditions. It seems reasonable to suppose that this is probable in some cases at any rate which is a further point in putting emphasis on the importance of early diagnosis.

The ultimate outcome, when immediate recovery results, supports this also. With early recognition and immediate operation the chance for good restitution of function on the affected side is excellent. Exactly the same arguments apply as those used to support the value of

early tapping in the more common serous effusion. Every day that the patient goes with fluid in the pleural cavity increases the chance of permanent changes in the lung—collapse and fibrosis—favors the thickening of the pleura, and tends to cause shrinking of the side and drooping of the shoulder. This is emphasized by the finding of fibroid change in the lung and marked thickening of the pleura in a patient dying on the twenty-fourth day.

The ultimate results in this series were good. There was no instance, in any patient who was examined some time after recovery, of bronchiectasis or marked fibroid change. The usual condition was slight shrinking on the affected side, the average difference in the measurement being less than an inch, with some drooping of the shoulder, dulness and rather diminished breath sounds at the base. This was not always the case, some patients showing practically no change. One patient who had empyema on the right side in 1890, returned with a second attack of pneumonia in 1895. The lower right lobe was involved again. As a rule, with early operation especially, the outlook in children for good ultimate recovery of function is excellent.

How frequently is an empyema absorbed? In the literature one finds considerable diversity of opinion as to the frequency of absorption of an empyema. It is usually considered that in a child there is more possibility of absorption than in adults, and hence, the advice sometimes given to try aspiration in a child before advising operation. There was only one instance in this series in which absorption occurred. The history is as follows:

Med. No. 20,699. The patient was a male, aged 15 years, white, and a tailor by occupation. He was admitted on the third day with involvement of the lower and middle right lobes, and subsequently of the upper right lobe. The physical signs were rather puzzling, and on the fourth day, a needle was inserted in the right back and 5 cc. of turbid fluid obtained. This showed a distinct sediment, and on examination was found to contain many pus cells and pneumococci. On the following day the procedure was repeated with the same result. On the eighth day the temperature began to fall. The breath sounds were very tubular, and many fine crackles were heard. The temperature fell by lysis and reached normal on the tenth day. The patient made a good recovery and was discharged well on the twenty-fifth day. The pulse rate was from 100 to 130 during the pneumonia, and afterwards normal. The respirations fell to normal with the temperature and remained there.

Such results must be regarded as exceptional and certainly should not be used as an argument for delaying operation.

*Diagnosis.*—This must be regarded as the most important aspect of the discussion of empyema. Recognized early and treated properly, the outlook, both immediate and ultimate, may be regarded as good. Every day that the condition persists renders the chances poorer. As regards the immediate outcome, there is always the danger of some complication such as pericarditis, meningitis or septicæmia, not forgetting the effect on the general condition and resistance of the patient. As regards the ultimate restoration of function if the patient recovers, every day of delay lessens the chance of this being complete. Shrinking of the affected side, drooping of the shoulder, marked thoracic deformity, thickening of the pleura, more or less fixation of the lung in a collapsed state, and fibroid changes are undoubtedly favored by long continued empyema. Given early recognition, and it may be said with fair certainty that these can be avoided.

There is but one symptom which may be said to be always present with empyema, and that is fever. This, in the majority, is more or less continuous with that of the pneumonia; if the temperature returns to normal it rarely remains there for more than a day or two. Therefore, it is a good rule to consider empyema as a possibility—perhaps better a probability—in every instance in which fever persists after the attack of pneumonia. The most common conditions causing fever are (1) empyema, (2) delayed resolution, (3) tuberculosis, either coexistent with a lobar pneumonia, or a tuberculous pneumonia, wrongly diagnosed, (4) some complication, and (5) a slight gradual extension of the pneumonia process.

(1) Empyema. Speaking more especially about the *early diagnosis,* it is evident that no physical sign can be regarded as constantly present. We must, therefore, be prepared to have our suspicions aroused rather than our fears confirmed by them. Of the signs which were of most value in the early recognition in this series, decrease in the vocal fremitus, changes in the percussion note and especially alterations in the breath and voice sounds were the most important. It must be remembered that the decrease in the vocal fremitus may not be marked, certainly for some days, and that too much weight must not be attached to its retention as evidence against the presence of empyema. Change in the percussion note if present may be of the greatest help. An increase in the dulness, and especially a certain wooden quality, are most important. With this goes the feeling of resistance; there is something about it which can hardly be described in words and yet

is most suggestive if present. Perhaps on the whole the results of auscultation give the greatest aid. Suppression of the breath sounds and a peculiar nasal quality of the voice sounds are the changes which are most suggestive.

With the variability in the physical signs, emphasis is laid on the advisability of employing the most certain means of diagnosis, namely, the use of the needle. It is well to use rather a small needle, not from any special advantage in that, but because with it one is likely to hesitate less about frequent needling. Then too, in early stages the fluid is not likely to be very thick and there is rarely any difficulty from the needle being stopped. Every precaution should be taken to avoid infection. There should be no hesitation about using the needle repeatedly. It is a good lesson to see how in some foreign clinics the needle is used for diagnosis in the same way as many of us use a stethoscope. It may be necessary to introduce the needle in several places; in some cases of this series half-a-dozen punctures were made before pus was obtained. The use of the X-rays may be of help in cases of considerable amounts of exudate, but in the very early stages a great deal of certainty can not be expected. However, in a doubtful case, if the patient's condition does not forbid it, the fluoroscopic examination should be made.

(2) *Delayed Resolution.*—As a rule this is recognized without great difficulty. The mistake of considering empyema to be delayed resolution is more common than the contrary. If the physical signs are doubtful, puncture generally gives assistance. The feeling communicated by the needle, introduced into the consolidated lung, is fairly characteristic.

(3) *Tuberculosis.*—This occasionally gives considerable difficulty. The persistence of signs may suggest empyema, although the distinction as a rule is easy, or, if tuberculosis is present and recognized, the signs of empyema may be thought to be those of thickened pleura. One case may be quoted in which the presence of tuberculosis led opinion astray for several days:

Med. No. 10,963. The patient, a colored man, aged 32 years, was admitted on the third day with involvement of the lower left lobe. On the tenth day the temperature fell, and continued low until the fifteenth day when it became higher and there were signs of involvement of the upper left lobe. There was tubular breathing and a loud friction rub, especially over the lower thorax. On the eighteenth day, large numbers of tubercle bacilli were found in the sputum. In view of the anomalous course, it

was considered that the diagnosis of lobar pneumonia was wrong and that the condition had been tuberculous from the beginning. Tubercle bacilli were found repeatedly. The signs persisted on the left side, and on the thirty-second day aspiration was done with a negative result. After this the patient had marked œdema of the left axillary and pectoral regions and of the left leg. This cleared and later an abscess formed in the left thoracic wall, which was drained and did not communicate with the pleural cavity. The signs over the left lung were puzzling. There was restriction of motion, increased vocal fremitus, dulness and harsh breath sounds accompanied by many coarse rales. In view of the evident diagnosis of tuberculosis the signs were regarded as due to that. Finally puncture showed pus containing pneumococci; the patient was operated on and made a good recovery. It may be said that the physical signs were anomalous, and suggested any condition other than empyema.

(4) *Complications.*—These should rarely be a cause of confusion. It is evident that abscess or gangrene might suggest empyema. No rules can be laid down which would apply to all cases. Endocarditis or pericarditis should be easily recognized.

(5) *Extension of the Pneumonic Process.*—This should be easily recognized from the physical signs. This and the occurrence of complications are likely to be considered on account of the persistence of fever, but are not very readily confused with empyema.

*Treatment.*—As a rule this must be surgical, and the earlier it is carried out the better. How long we are justified in waiting to see the result of aspiration is a question that may be asked. As a rare result we may have absorption, but it may be a question whether this might not have occurred without aspiration. Some authorities consider that aspiration is more likely to be successful in children than in adults. Certainly there should not be a delay of more than two or three days before operation, if the symptoms persist after aspiration. In all but one of this series, in which aspiration was tried, operation had to be done subsequently.

It may be said that no condition is too desperate to contraindicate operation. We had a notable example in the hospital. A child with empyema was brought in from the country, being carried in her father's arms. When they reached the hospital the child was moribund, had a grayish hue, and it seemed hopeless to attempt any treatment. However, the child was hurried to the operating room, although death seemed likely before there was time to get there, and without any delay the pleural cavity was opened. An enormous amount of pus escaped, the condition improved at once and the child made a good recovery.

As a rule the operation can be done under local anæsthesia, or with this and a few whiffs of chloroform. The main thing is to get thorough drainage, and it is usually better to resect a portion of a rib than to attempt to drain through an intercostal space. It is better not to irritate at the time of operation. The surgical details do not require discussion.

If the condition persists and shows no signs of progress, it is well to try the treatment by vaccines. Whether this would be of value in the early acute stage is as yet uncertain.

It is well to keep the patients out of doors as much as possible, and give large amounts of nourishing food. If there be anæmia iron and arsenic are indicated.

The after treatment is important. Every effort should be made to secure as good expansion as possible on the affected side. In children the use of the Wolff bottles is very helpful. They can be started at these quite early and encouraged to use them every day. The same may be used by adults, and in addition, as soon as they are about, they should be started at the exercises which secure expansion on the affected side. Of these perhaps the best is that in which the patient sits sideways on a chair with the sound side against its back, which is firmly held against the thorax and so acts as a splint to prevent expansion on that side. Of course discretion must always be used as to when the exercises should be begun, and how energetically and frequently they should be carried out. After recovery the patient should carry on some form of respiratory exercise for from six months to a year, unless there be definite reasons against this.

*Conclusions.*—The special impressions which are made by the study of this series are:

1. In the majority of instances empyema may be regarded as a complication of pneumonia.

2. It occurs relatively much more often in the colored than in the white race.

3. Fever was the only manifestation always present.

4. The physical signs may be variable, and it is well to remember that vocal fremitus may be retained, even with a considerable amount of exudate.

5. Of the physical signs, changes in the breath and voice sounds were the most useful single manifestation in diagnosis.

6. The importance of repeated needling in all cases which are in doubt.

# PERIPHERAL VENOUS THROMBOSIS IN PNEUMONIA WITH REPORT OF THREE CASES AND A REVIEW OF THOSE PREVIOUSLY RECORDED.

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During the past decade our attention has been especially called to venous thrombosis, as occurring in connection with certain infectious diseases and as following some abdominal operations. A considerable number of cases have been reported where it has occurred in influenza and typhoid fever, but there are few references to its occurrence in pneumonia.

Da Costa (1) reported his first case in 1894 and considered it unique. Four years afterwards he gave the histories of 2 more cases and succeeded in finding 6 previously published (2). A little later, Welch (3) was able to add 14 more, making the total number of cases 23. But previous to these, Monod (4), Valette (5), Hayem (6 and 7), and Lande (8) had reported cases that appear to have escaped detection in the reviews of the literature upon this subject. Since then a number of additional cases have been described. Jones (9), Clark (10), and Hall (11) each have placed 1 case on record, and Gauchet (12) Sears and Larrabee (13) have added considerably to the list.

Gauchet made venous thrombosis in pneumonia the subject of his thesis and gave an abstract of 21 cases. Some of these should be excluded, however, as they were not due to typical lobar pneumonia, but to influenza. I, consequently, have not added these to my list and have omitted the mention of 2 others for different reasons. In 1 of of the latter no *peripheral* venous thrombosis was found and in the other there was a history of syphilis and mitral stenosis, so that the thrombosis was possibly not due to the pneumonia. (There remains then only 1 of Gauchet's cases which I have not included in my group. Much of the ground traversed by his thesis had been gone over by me before my attention was called to his work.) Sears and Larrabee found 10 instances of venous thrombosis in 949 cases of pneumonia

treated at the Boston City Hospital. More recently Monmeneu (14), Obrecht (15), Widal, Lemiére, and Gadaud (16), Coleman (17), Miller (18), Person (19), Pierre (20), and Gaultier (21) have increased the list to 51 cases, which added to the 3 detailed in this report, makes the total number 54. The labors of Obrecht and Pierre are embodied in theses, in which there are very careful studies of the subject.

The following 3 cases are the only ones that have been met with in a series of 658 pneumonia cases treated at the Johns Hopkins Hospital from May 15, 1889, to May 15, 1905.

CASE I.—*Pneumonia of both lungs; crisis on the 9th day; accompanying pleurisy of both sides; second attack of pneumonia, 7 days after the crisis, of 5 days duration; thrombosis of right popliteal vein 28 days after the crisis and 6 days after the termination of the second pneumonic attack; gradual recovery.*

X., aged 21 years, (Hospital No. 25,220), was admitted to the Johns Hopkins Hospital January 9, 1899, complaining of pain in the left side, cough, and loss of appetite.

*Family History.*—Mother died of pneumonia, aged 39 years.

*Past History.*—Whooping cough as a child. Measles a year ago, slight attack. Malaria in 1898, quotidian in type. Was living at Halifax, N. C., at the time. Gonorrhea 6 months ago, no complications. Moderate smoker and drinker. Had worked at dredging.

*Present Illness.*—Two weeks before admission caught cold and 4 days ago had a severe shaking chill which lasted about 10 minutes. "High fever" came on then and has since continued. A severe headache was also complained of at this time, which obliged him to go to bed, where he remained until he took the steamer for Baltimore 2 days ago. On the day of arrival he felt a severe dull pain in his left chest and abdomen, which has since persisted. It is not increased by deep inspiration or coughing. Has had chilly feelings every day since the onset of the chill. His cough is dry and hacking and 4 days ago he first noted that his expectoration was slightly blood-tinged. His bowels have been constipated since the onset of his illness.

*Physical Examination.*—The patient was a well-nourished, powerfully-built negro. Was in a profuse perspiration during the time of the examination. The respirations were a trifle rapid and there was some dilatation of the alæ nasi. The lips and mucous membranes were of good color. The tongue was coated with a thick white fur.

*Thorax.*—Well-formed, symmetrical. The costal angle was normal. The expansion was limited, the right side moving more than the left.

*Lungs.*—In front the percussion note on both sides was clear, being slightly impaired over the upper left. The stomach tympany extended

high up into the left axilla. Over the left side the breath sounds were very feeble and suppressed in quality. The same condition was noted in the left axilla. Over the right side the sounds were louder and harsher, and the expiration was somewhat prolonged. In the lower left axilla an occasional very fine râle was heard at the end of inspiration. Behind, the note on the left side seemed somewhat impaired and the breath sounds had a distant quality except in the interscapular region, where distinct tubular breathing was audible. In the lower right side there was impairment of the note and below the angle of the scapula fairly well-marked tubular breathing.

*Heart.*—The point of maximum cardiac impulse was visible and palpable in the 5th interspace, 8.5 cm. from the midsternal line. The cardiac dulness was not increased. The sounds were loud and somewhat booming. No murmurs were heard. The pulmonic second was somewhat accentuated.

*Abdomen.*—Negative.

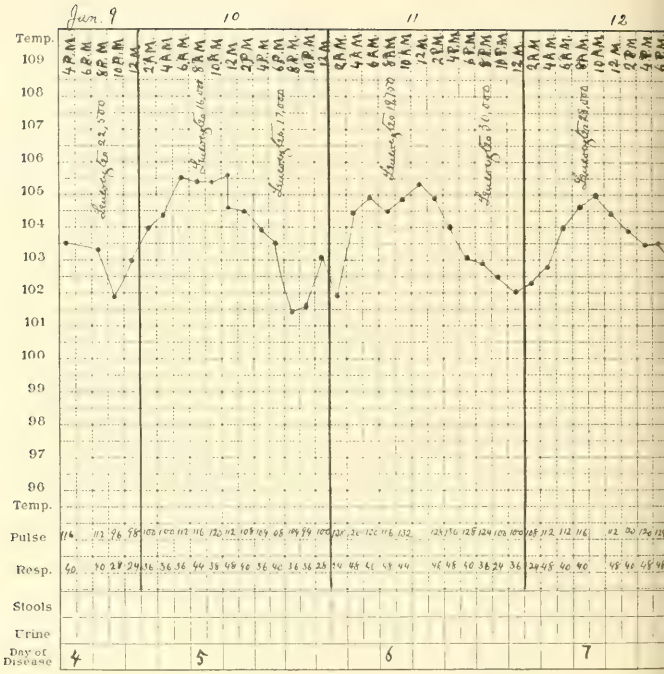
*Extremities.*—Negative.

The examination of the sputum showed it to consist of a large amount of rather thick tenacious, whitish fluid streaked with blood. Microscopically many epithelial and red blood cells were seen, as well as a few leucocytes. Many bacteria were also observed, being mostly diplococci and streptococci.

On the next day a well-defined friction rub was heard in the lower left axilla and here the breath sounds were very much suppressed. The percussion note was impaired over the whole left side, but no other change was noted.

On the day following, January 12, his condition seemed worse. His respirations were shallow and very labored, 60 to the minute. His tongue was deeply coated with a thick white fur. He complained much of sharp pain in the left lower axillary region. The pneumonic process seemed to involve the whole left lung and the right lower lobe. A loud friction rub was audible in the left lower axilla.

Dr. Futcher made the following note on January 13: Patient's temperature remains elevated, ranging between 103° and 105° F., the pulse is rapid, small in volume, and easily compressible, 35 to the quarter; there is no marked respiratory distress; the respirations are 52 to the minute. The right side of the chest moves distinctly more than the left. In front the note is rather hyperresonant over the right side and upper axillary regions, but flatness exists below the 7th rib in the mid-axillary line. There is also an impairment of the note over the submammary region. The breath sounds are rather exaggerated over the upper right front, but over the submammary and lower axillary regions they are much enfeebled, distant, but not tubular. The voice sounds are slightly diminished. On the left there is distinct impairment of note in the supraclavicular fossa and over the upper front as low down as the IV rib, and the vocal fremitus is here perceptibly increased. The breath sounds have a


Jan. 9
10
11
12
Temp.
Pulse
Resp.
Stools
Urine
Day of Disease
4
5
6
7

CHAR

13
14
15
16
12 M.
2 P.M.
4 P.M.
6 P.M.
8 P.M.
10 P.M.
12 M.
2 A.M.
4 A.M.
6 A.M.
8 A.M.
10 A.M.
12 M.
2 P.M.
4 P.M.
6 P.M.
8 P.M.
10 P.M.
12 M.
2 A.M.
4 A.M.
6 A.M.
8 A.M.
10 A.M.
12 M.
2 P.M.
4 P.M.
Leucocytes 21,500
Leucocytes 18,400
Leucocytes 17,250
Leucocytes 11,000
Leucocytes 12,250
Leucocytes 6,250
Chills
9
10
11

somewhat distant tubular quantity and a distinct pleuritic friction rub is audible over this area as well as in the upper axillary and intermammary regions. Throughout the submammary and lower axillary regions the note is markedly tympanitic and the breath sounds are enfeebled and of a distant tubular quality. In the back there is an impairment of resonance over the area occupied by the right lower lobe and tubular breathing is well heard, although somewhat less distinctly over the lower subscapular area. The note is practically flat over the whole left back and tubular breathing can be everywhere well heard, but it is less distinct over the lower subscapular region. There are a few moist râles to be heard on inspiration. There are no murmurs over the heart, but at the apex a pleuro-pericardial friction rub can be heard. The pulmonic second is markedly accentuated.

The temperature fell on this day to 97.2° at 12 midnight,—a fall of 8.2° in 16 hours. Four hours later it had fallen still lower and was 96.2°. From this time on the temperature began to rise and at 11 a. m. on the next day, when it was 98.2°, the patient had a distinct chill. The maximum rise was reached at 12 midnight, when the temperature was 104.9°. In 4 hours there began a gradual fall again, the temperature reaching 96.2° at 4 p. m. on January 15,—a fall of 8.7° in 12 hours. The drop was accompanied by a profuse perspiration. Later in this day another rise was noted, the temperature at 4 p. m. being 102.7°, but it soon fell, and in the early morning of January 16, was subnormal (see Chart I).

The lungs gradually showed signs of clearing, but symptoms of pleurisy still remained at both bases. There was dulness and a nasal quality to the voice sounds on both sides and an occasional to and fro friction rub was audible in the left lower axilla. No movable dulness was made out. The resolution process seemed very slow, but the patient continued to do well. His appetite was returning and he suffered no pain on breathing. On January 21 Dr. Osler noted that there was still impairment over the left lower lobe on percussion, but the vocal fremitus could be well felt here. The breath sounds were yet a little tubular at the angle of the scapula.

Two days later on January 23, the patient complained of pain in his left side and began to spit up a considerable amount of blood. At 8 p. m. on this day his temperature rose to 104.5°. At midnight he had a chill and the temperature the following morning remained elevated. The sputum became very tenacious, distinctly blood-streaked, and in places prune-juice in character. There was no herpes. The respirations were somewhat hurried and the alæ nasi seemed to dilate a little with each inspiration. No new pneumonic process could be found in the lungs, nor was there any change in the lung condition, save that the friction rubs were no longer audible, except the pleuro-pericardial rub, which was still heard over the heart at the apex. The pleuritic second continued to be markedly accentuated and was somewhat reduplicated. The temperature fell in 5 days to about normal. On the day following this fall Dr. Osler noted

that the resonance in the left front and axilla was clearing, but flatness still persisted in the left back below the middle of the scapula. Fremitus, however, was here well felt, but the breath sounds were distant and suppressed—not distinctly tubular. There were a few crackles on deep inspiration and a soft friction rub in this area. No profuse perspiration accompanied the fall in temperature.

On February 3, 4 days later, he complained of pain in his right leg, principally in the calf. There was nothing to be seen on inspection and nothing to be felt in the vessels of that leg. The temperature rose on this day to 100.8°. Six days later he was allowed to get up out of bed, as he no longer complained of this symptom and the examinations continued to be negative. On the evening of that day he called attention to the swollen condition of his right leg. He complained of pain in the popliteal space and calf. On examination the lower right leg and thigh seemed a trifle swollen. They pitted easily on pressure. There was no tenderness or swelling to be made out along the course of the blood vessels.

He was kept in bed and warm applications of the lead and opium lotion were applied to relieve the pain and reduce the swelling. The latter, however, still persisted. Dr. Futcher's note, 15 days later, reads as follows: "There is a distinct swelling of the right thigh and leg as well as the dorsum of the foot. It is most marked between the knee and ankle. The superficial temperature is distinctly elevated and the skin easily pits on pressure. Some tenderness can be made out on palpation over the calf muscles, but there is no evidence of thickening or tenderness over the femoral vein in Scarpa's triangle or along its course." The swelling was later considerably reduced by the application of a tight bandage.

On March 4 he complained of a sore throat and his temperature rose to 102.2°. Just before this rise he had a slight chill. An examination of his throat showed the pharynx was reddened and injected and both tonsils were considerably swollen. The chest, heart, and abdomen were negative on examination. By appropriate remedies his sore throat was relieved and in 3 days his temperature was normal again. A week later, on March 11, at his urgent request, he was discharged, though the right leg was still larger than the left and pitted readily on pressure. The following measurements were then taken from the following distances from the patella.

| | Right leg. | Left leg. |
|---|---|---|
| 13.5 cm. | 33.8 cm. | 32.0 cm. |
| 20.4 " | 28.3 " | 27.5 " |
| 36.3 " | 23.0 " | 21.5 " |

An examination of his lungs at this time showed only a slightly diminished vocal fremitus over the right front and axilla.

*Leucocytes:*

| | | | | | |
|---|---|---|---|---|---|
| Jan. | 9 | a. m. | 16,000 | p. m. | 17,000 |
| " | 10 | p. m. | 22,000 | | |
| " | 11 | " | 19,750 | " | 30,000 |
| " | 12 | " | 28,000 | " | 28,000 |
| " | 13 | " | 23,000 | " | 21,500 |
| " | 14 | " | 19,400 | " | 17,250 |
| " | 15 | " | 11,000 | " | 12,250 |
| " | 16 | " | 6,200 | | |
| " | 23 | " | 10,000 | | |
| " | 24 | " | 9,500 | | |
| " | 25 | " | 6,000 | | |
| " | 26 | " | 6,500 | | |

*Urine Examination.*—On entrance the urine was reddish amber, cloudy, 1023, acid and negative for sugar and albumin. Microscopically a few pus cells and red blood corpuscles were found. The other examinations did not vary much from that above given.

*Temperature.*—See Chart I for the first 10 days. From January 16 to January 23 it varied from 98.2° to 100.4°, generally rising a degree or more towards evening. See Chart II for the next 5 days. After this it varied from normal to 100.4°, but was generally below 100°. On February 3 it rose to 100.8°. From February 4 to March 3 it was about normal and remained then slightly subnormal until his discharge.

He was admitted again to the Johns Hopkins Hospital 7 days later (Hospital No. 25,909) complaining of a swollen right leg. He had not gone back to work until 3 days after his discharge. He then got a job of unloading a box car and had worked at this for 3 days. On the morning of the 4th day he complained of pain in the sole of his right foot and popliteal space and noted his right leg was much swollen. He came to the hospital later in the morning.

The physical examination revealed nothing of especial interest, save that the right leg was swollen and markedly œdematous. The surface temperature was slightly elevated and pitting was easily obtained on pressure. There was slight tenderness in the popliteal space, but no thrombus could be felt here or along the course of the veins. The temperature rose to 99.6° at 6 p. m. on March 9, but was soon normal again and so remained until his discharge March 25. At this time the swelling of the leg had entirely disappeared. The treatment consisted in the application of a tight-fitting bandage.

The marked variations in the temperature on January 13, 14, and 15 may be variously interpreted. We regard the fall of temperature on the first day named as a pseudo-crisis. The real crisis seems to have occurred on the evening of the 2d day when the patient perspired most profusely. The 3d rise of temperature on January 15, may be looked upon as a post-critical rise. The chill on January 14 may have denoted a slight further extension of the pneumonic process.

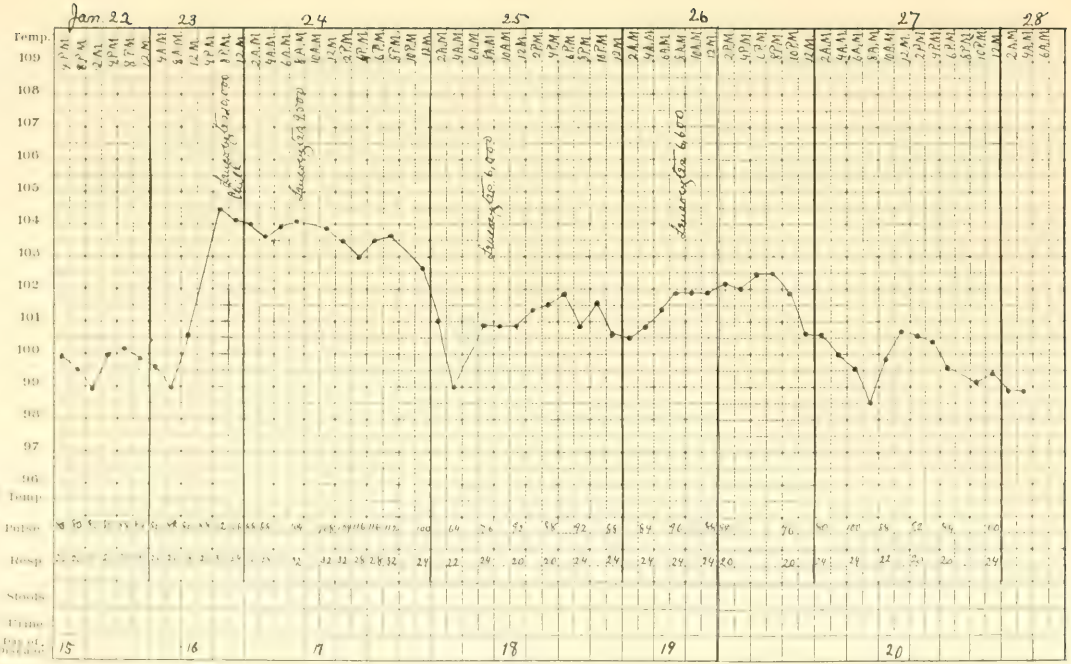



CHART II.—Case I.

Though many would take the rise in temperature on January 23 and its subsequent elevation for 5 days as an example of a relapse, yet it might better be regarded "as an instance of an anomalous course of delayed resolution." (22). It was attended with prune-juice expectoration and as no definite lung lesion was found, the process might be considered centrally located. As may be noted it was not accompanied by a leucocytosis.

Case. II.—*Right lobar pneumonia; thrombosis of the right internal saphenous vein on the 6th day of the disease; death 6 days later.*

X., aged 63 years, (Hospital No. 33,727), was admitted to the Johns Hopkins Hospital February 1, 1901, complaining of feeling badly all over and of a dry mouth.

*Family History.*—Negative.

*Past History.*—Measles, mumps, whooping cough, and scarlet fever as a child. Typhoid fever 24 years ago and malaria in the fall of the year when a young man. The chills occurred every other day. He was living in Kent County, Maryland, at the time. One-sided hemiplegia (side not stated) about 43 years ago, which left him considerably disabled for a long time. Had had 2 or 3 attacks of rheumatism many years ago and had been confined to bed with them. Chancre when 35 years old, no secondaries. Gonorrhœa many times, never any complications. Had been a heavy drinker from his youth up and had frequently been intoxicated. Was formerly a heavy user of tobacco. Was a cooper by occupation.

*Present Illness.*—About 10 days before admission complained of a pain in his right side. It was not of very long duration, but about this time he began to cough. His cough was dry and hacking in character and was accompanied by slight expectoration which was never blood-tinged. In spite of these symptoms he kept about, but had done no work for the past 3 weeks. Saturday, 2 days ago, he had a severe shaking chill which obliged him to go to bed, where he remained until he came to the hospital.

*Physical Examination.*—The patient was a fairly well-nourished old man with lips and cheeks slightly cyanotic. The respirations were 38 to the minute, the temperature 101.4° and the pulse 120 to the minute, of good volume, fair tension and regular in force and rhythm. The vessel walls were considerably sclerosed. His tongue was coated with a thick white fur. The sputum was frothy, tenacious, and slightly rusty in places.

*Thorax.*—Barrel-shaped with limited expansion,—a little less on the right side.

*Lungs.*—On percussion the note on the right side in front as low down as the fourth rib and in the upper axilla was distinctly impaired, but on the left side and lower right axilla it was hyperresonant. The breath sounds at the right apex were harsh, expiration was prolonged and fine and coarse crackling râles were heard. From the first interspace down to the nipple intense tubular breathing was noted with numerous crepitant râles on inspiration. Over the lower left front and axilla the breath sounds were harsh and wheezing with a few sibilant râles on inspiration. Behind the

note was resonant on the two sides with harsh respiration accompanied by crepitant râles, except on the right side from the supra-clavicular fossa to the level of the 4th vertebra where tubular breathing was heard which extended into the right axilla.

*Heart.*—The relative cardiac dulness was diminished. The point of maximum cardiac impulse was in the 6th interspace, 11 cm. from the mid-sternal line. There was a faint systolic murmur audible at the apex, but the 2d sound was clear. The sounds at the base were somewhat feeble but clear.

*Abdomen.*—Negative.

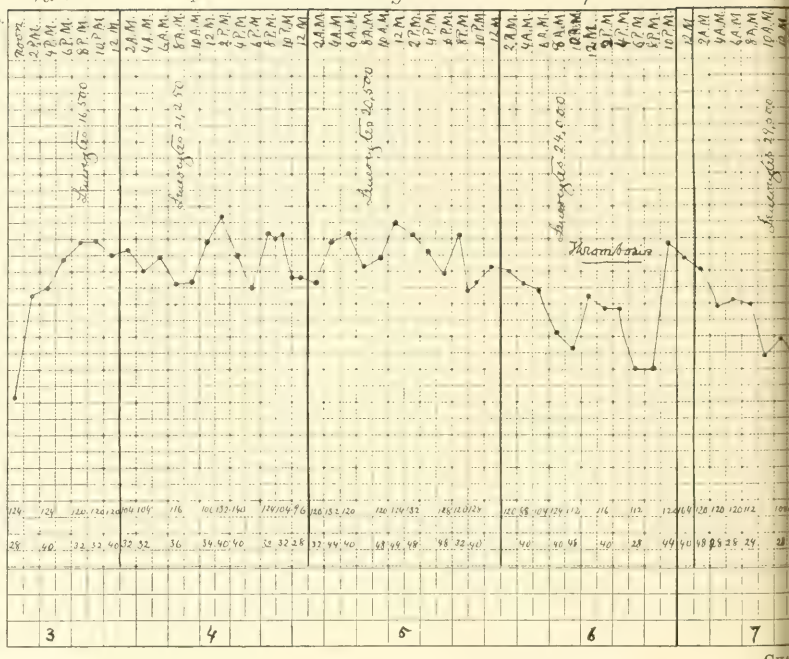
*Extremities.*—There were marked varicosities in the veins on the inner sides of both legs.

*Blood Examination.*—Red blood corpuscles 3,996,000; white blood corpuscles 16,500; hæmoglobin 50%.

On the next day his condition seemed to be fairly good, though the respirations had arisen to 40 to the minute and the pulse to 144. There was no cyanosis. The flatness and tubular breathing was limited to the upper and middle right lobes. On the day following, February 4, the varicose veins of the right leg began to cause considerable pain, especially above the knee, where they were slightly red and quite firm and tender on palpation. His temperature rose on this day to 102.8° at 10 p. m. The lower right lobe posteriorly now began to show signs of involvement. The note was markedly impaired, and on auscultation the expiration was prolonged and a few moist râles were heard on inspiration. The heart sounds were feeble but clear. Later in the day the pulse became very irregular, there being short periods of apnœa of 8 to 15 seconds between every interval of from 4 to 8 respirations. The patient was quite irrational.

On February 5, it was noted in the history that the patient had perspired very profusely the day previous and on that day. Dr. Futcher made the following note on February 6; "Patient somewhat cyanotic and is perspiring freely. Pulse fair volume and tension, regular, 120. Respirations rather irregular, suggestive of Cheyne-Stokes type. Periods of apnœa of several seconds duration. Dull mentally, but responds to questions. There is considerable impairment of the note over the right subscapular region and numerous fine râles are heard at the end of inspiration. The tubular breathing is less marked over the left upper lobe. No inequality of pupils is noted. There is no especial stiffness of the neck muscles. The right thigh and leg present an extraordinary condition. The internal saphenous is distinctly visible throughout, the size of one's little finger. It is cord-like on palpation and is apparently deeply thrombosed. There is slight reddening of the skin along its course. The superficial veins of the leg below the knee are also dilated and apparently markedly thrombosed. At the inner margin of the left popliteal space there is a mass of varicose veins which are also apparently thrombosed."

On the next day œdema of the right foot and lower two-thirds of the leg was observed. The surface temperature was not lowered. Two days later the internal saphenous throughout its course seemed less distinctly


Feb.
2
3
4
5
Temp.
109
108
107
106
105
104
103
102
101
100
99
98
97
96
Temp.
Pulse
Resp.
Stools
Urine
Day of Disease
3
4
5
6
7
Leucocytes 16,500
Leucocytes 24,250
Leucocytes 20,500
Leucocytes 24,000
Leucocytes 29,000
Thrombosis

6
7
8
9
10
Discharged 19,500.
Discharged 24,000.
Discharged 24,800
Discharged 13,200
Discharged 24,500
Death 6.30 A.M.
8
9
10
11
12

visible and a line of yellowish red pigmentation was here seen. The marked œdema of the right leg and foot still persisted. They were also cyanosed in appearance.

The patient gradually sank, his respirations became very shallow and the pulse very small in volume and thready. The lung lesions showed signs of clearing, the breathing becoming less tubular and numerous coarse moist râles being heard. He was infused with saline solution, but he did not improve after it and died quietly at 6.30 a. m. on February 10.

*Leucocytes:*

| | | |
|---|---|---|
| Feb. | 1 | 16,500 |
| " | 2 | 21,250 |
| " | 3 | 20,500 |
| " | 4 | 24,000 |
| " | 5 | 29,500 |
| " | 6 | 16,500 |
| " | 7 | 24,000 |
| " | 8 | 13,200 |
| " | 9 | 24,500 |

*Cultures.*—Five cultures were made during the patient's illness. Three from the blood, one from the spinal fluid and one from the thrombus. They were all negative for pneumococci.

*Urine Examination.*—On entrance the urine was reddish yellow, cloudy, 1020, and acid, negative for sugar, but contained a trace of albumin. There was no sediment. Microscopically a few hyaline and granular casts were seen, as well as a few leucocytes and triple phosphate crystals. There was no especial change in the urine while the patient was in the hospital.

*Temperature.*—See accompanying Chart III.

Autopsy (Dr. MacCallum). *Anatomical Diagnosis.*—Unresolved pneumonia of right lung; compensatory emphysema of left lung; thrombosis of right internal saphenous vein; œdema of right leg; fatty metamorphosis of liver, anæmic infarction of spleen; fragmentation of myocardium.

Body of a somewhat emaciated man, 165 cm. long; rigor mortis well marked; right leg very much larger than left, very œdematous; saphenous vein can be felt as a prominent hard cord; 1 or 2 decubitus ulcers over prominent parts of back. The peritoneal cavity is very dry; peritoneal surfaces are smooth; mesenteric lymphatics rather opaque and yellowish; chyle ducts are apparent here and there as white lines.

*Pleural Cavities.*—The left is partly obliterated by old adhesions; the right shows fresh fibrinous adhesions.

*Pericardial Cavity.*—A small quantity of blood-stained fluid is here contained and both layers of the pericardium are smooth, with brownish discolorations; the epicardium shows a few tendinous patches over the right ventricle; the coronary arteries are somewhat thickened and tortuous, and show 1 or 2 epicardial fibroid nodules.

*Heart.*—The tricuspid and pulmonary valves are delicate; the mitral

valve is also delicate, but the aortic leaflets are slightly thickened at their margins though apparently competent; the myocardium is very soft, rather grayish in color; the coronary arteries are fairly natural. The heart weighs 300 gms.

*Left Lung.*—The surface is everywhere smooth, except for old adhesions; the lung substance is greatly insufflated. It shows no consolidation.

*Right Lung.*—Considerably enlarged and bound down to the ribs and diaphragm by old as well as fresh adhesions. On section the upper and lower lobes are quite consolidated except for scattered areas of air containing lung, the areas being sharply limited; the cut surface is quite smooth and slippery; it is of a reddish gray translucent appearance; in the lower lobe the consolidation is somewhat less firm, and although very diffuse leaves numerous small irregular air-containing areas; the alveoli are very large in the lower lobe, giving a somewhat ragged appearance to the cut surface which has not the granular field of a pneumonic lung. Throughout this lower lobe yellow points of opacity can be seen scattered among the reddish-gray substance; the lung everywhere is very œdematous; in the anterior portion the gray translucent areas are even firmer and more sharply limited from the air-containing portions; the bronchi are not especially inflamed, although somewhat red.

*Spleen.*—Weight 70 gms. The capsule is somewhat thickened by opaque whitish patches, all of which project slightly above the surface. On section these whitish patches are found to correspond to pale, opaque, whitish areas, somewhat wedge-shaped. Each of them is surrounded by a zone of deep red, from which they are sharply defined; the splenic substance is somewhat atrophied; the trabeculæ and vessels are very distinct.

*Liver.*—Weight 1850 gms. Its surface is everywhere smooth; the margins are thick and rounded. On section the lobuli are very distinct, the marginal portions being of a pale yellow color.

*Kidneys.*—Weight of both 280 gms. The capsule strips off with some difficulty, leaving, however, an apparently smooth surface with occasional retention cysts. On section cortex about 6 mm. The epithelium is pale.

The examination of the other organs is negative.

The right saphenous vein is distended by a dark red thrombus mass.

The femoral vein contains only a post-mortem clot.

*Microscopical Examination.*—Sections of the heart show well-marked fragmentation; sections of the lung show in places a moderate increase of interstitial tissue and in places the alveolar tissue is almost wholly replaced. Some few alveoli contain a moderate number of polynuclear leucocytes and desquamated cells. Other sections show almost complete organization of the exudate and abundant desquamated cells in the remains of the alveoli. The spleen and kidney seem normal.

*Bacteriological Examination.*—The diplococcus lanceolatus and the staphylococcus pyogenes aureus were obtained from cultures taken from the lungs. The heart's blood showed the presence of the streptococcus pyogenes, while cultures from the thrombus in the saphenous vein, the spleen, the bile, the kidneys, and the urinary bladder were negative.

Case III.—*Left lobar pneumonia; severe infection; termination by lysis; thrombus of the right popliteal vein 6 days after patient's temperature was normal; gradual recovery.*

X., aged 27 years, (Hospital No. 37,464), was admitted to the Johns Hopkins Hospital January 4, 1902, complaining of pain in the side and fever.

*Family History.*—Negative save for some indefinite history of rheumatism.

*Past History.*—Measles as a child. Two previous attacks of pneumonia, the last one during the past winter. Indefinite history of rheumatism several years ago. Denies lues. Has had several attacks of gonorrhœa, no complications. Has been a hard drinker.

*Present Illness.*—Five days ago (Dec. 30) "he got wet and caught a heavy cold on his chest." The day following he had a slight chill and complained of pain in his side. Some cough, shortness of breath, and expectoration were additional symptoms. He did not notice whether his expectoration was blood-tinged. That night he had fever. Has had no nausea or vomiting. No herpes. Has been quite constipated since the onset of his illness.

*Physical Examination.*—The patient was a very well-nourished, muscular negro. His respirations were labored and shallow, with an occasional expiratory grunt. There was some dilatation of the alæ nasi and some cyanosis. His tongue was dry and coated.

*Thorax.*—Well-formed. The left side looked larger, but the expansion was equal.

*Lungs.*—The vocal fremitus was well felt on both sides in the front and in the axillæ. There were also some palpable rhonchi. The percussion note was resonant in these regions save in the posterior lower left axilla, where it was flat. The breath sounds were harsh and prolonged everywhere and almost tubular in the axillæ. Behind, the vocal fremitus was almost absent on the lower left side, where the note was flat on percussion. Above, there was a distinct impairment to the note of this lung. Over both sides the expiration had a curious jerky quality besides being harsh and prolonged. In the left interscapular region the breathing became almost tubular. It was typically so over the area of flatness on this side. Numerous coarse mucous râles were heard everywhere.

*Heart.*—The point of maximum cardiac impulse was felt in the 4th interspace, 7.5 cm. from the midsternal line. The sounds were somewhat indistinct, but seemed clear. There was a pleuro-pericardial friction rub to be heard over the cardiac area. The pulse was small in volume, of low tension and irregular. It was 120 to the minute. The vessel wall was distinctly felt.

*Abdomen.*—Negative.

*Extremities.*—Negative.

On the next day the patient seemed worse. The pulse was very small and irregular. The respirations were shallow and hurried, 72-76 to the

minute. The heart sounds were almost inaudible, no sound being heard at the apex. He was infused with 1100 cc. of saline solution, having been infused with 500 cc. the evening before. At the time of his 2d infusion the pulse could not be counted, but the heart beats numbered 41 to the quarter. The lung signs were unchanged except that the note had cleared up somewhat in the left lower lobe behind, but had become more impaired above, in the scapular region, where tubular breathing was heard. A well-marked friction rub was audible below the angle of the scapula and at the extreme left base. There was no delirium at any time. The sputum was small in amount, tenacious, not typically rusty, but more blood-streaked. Stained specimens showed pneumococci.

On the day following, January 6, Dr. Cole made the following note: "The patient is decidedly better this a. m. He has been sweating profusely and his temperature has fallen to 102°. The respirations are deeper and not quite so rapid. The pulse is much better in volume, still of rather low tension, but quite regular. The lung signs are about as yesterday. There is flatness and intense tubular breathing over the left lower back and axilla as far as the anterior axillary line. The breath sounds have a tubular modification over the upper left back. In front the percussion note is resonant and the breath sounds are harsh, with numerous râles. On the right side there is resonance below, but the percussion note is impaired in the infra- and supra-clavicular spaces, at the apex of the axilla and over the upper back. The breath sounds over these regions are harsh with numerous coarse râles. At the very apex of the axilla the breathing has a tubular modification. The heart sounds are much better heard than yesterday, although not yet audible at the apex. The pleuro-pericardial friction can still be heard.

He improved rapidly from this time on, though the lung seemed rather slow in clearing. The pleuro-pericardial rub was no longer audible 5 days later. On January 17, Dr. Osler noted that the apex beat was in the normal situation. The resonance in the left front and axilla had a tympanitic quality, shading off to dulness in the back. The breathing was distinctly tubular in the lower scapular region. The sputum was yellow and tenacious. No tubercle bacilli had been found on examination.

Four days later, on January 21, the 22d day of his illness, the patient's temperature reached normal. He seemed to be gaining in strength rapidly. For 2 or 3 days before January 25 pus had been seen in the patient's urine. On that day it was noted he had a purulent urethritis. Gonococci were found in the discharge. This flaring-up of an old attack of gonorrhœa was followed by an acute epididymitis 16 days later.

Six days after his temperature reached normal he complained of pain in the right lower leg. On examination an elongated very tender, cord-like swelling, the size of one's little finger, was found in the popliteal space. It was evidently a thrombosed vein and could be traced from there down the calf to nearly the lower third of the leg. There was no tenderness over the right femoral vein and no swelling of the lower leg.

His temperature rose on this day to 99°. On the next day he complained of pain in the right popliteal space. The cord-like popliteal vein was well felt.

On February 7, Dr. Osler observed that there was still more impairment of the note, on the left, in the mid-axillary line. There was also dulness on this side below and to the left of the scapula. The vocal fremitus was well felt. Later in the day a needle was inserted between the 7th and 8th ribs on this side, but no fluid was withdrawn.

He was allowed to get up and walk about on February 15. He then complained of pain in the right leg. Examination revealed a swollen tender popliteal vein, which had a cord-like feel. The swollen vein could be traced to the middle of the leg. Here some shot-like nodules, not especially tender, could be felt. The whole lower leg was slightly swollen and pitted on pressure at the ankle. No tenderness was noted over the femoral vein. In 2 days the swelling had become considerably reduced in size and was no longer painful.

He later experienced some inconvenience from "vaccination, as he had a marked 'take'," but was only in bed a short time from it. He was discharged March 4, at which time it was noted that his lungs were clear, though a pleuro-pericardial rub could still be heard in the 2d and 3d left interspaces. His leg was neither swollen nor painful.

*Leucocytes:*

| | | | |
|---|---|---|---|
| Jan. 4 | 26,700 | Jan. 20 | 5,400 |
| " 7 | 8,700 | " 21 | 5,200 |
| " 8 | 14,000 | " 23 | 8,400 |
| " 9 | 22,000 | " 28 | 5,100 |
| " 10 | 17,000 | Feb. 1 | 7,900 |
| " 12 | 18,000 | " 15 | 7,200 |
| " 13 | 15,700 | " 18 | 8,850 |
| " 14 | 10,600 | " 21 | 7,000 |
| " 18 | 10,000 | | |

*Cultures.*—Two cultures were made during his illness from his blood. They were both negative for pneumococci.

*Blood Examination.*—February 4. Red blood corpuscles 4,964,000; white blood corpuscles 9900; hæmoglobin 81%.

*Urine Examination.*—On entrance the urine was red, cloudy, 1015, and acid, negative for sugar, but contained a trace of albumin. Microscopically numerous finely granular, and a few hyaline casts were seen as well as some red blood corpuscles, leucocytes, and epithelial cells. The chlorides were much diminished. There was no special change in the urine except at the time stated in his history, when numerous pus cells were found in the urine.

*Temperature.*—On admission the temperature was 104.2°. It rose gradually to 106.5° at 4 a. m. on January 5, but then fell to 102° at 8 p. m. on that day. It varied now between this point and 104.5° at 4 p. m. on

January 9. From this time on it fell slowly to 100.8° at 10 a. m. on January 11, and varied then between this point and 103.4° on January 13, coming down gradually by lysis. It was subnormal for the first time at 6 a. m. on January 21. It then stayed about normal until the day of the thrombosis, when the temperature rose to 99°. On February 1, when a left epididymitis was noted, there was a rise to 103.7°, followed by a slow fall to 99.2° at midnight. From this time on to February 8 there were almost daily rises, 102.2° being the highest point reached. On February 8 his temperature reached normal. His fever from Feb. 1 on was doubtless due to his epididymitis. From February 8 to February 21 he had occasional slight elevations of temperature, but on the latter day the thermometer registered 103.2°. This rise was evidently due to his vaccination, as he had a marked "take." His temperature fell to normal on the following day and there were no subsequent rises.

## ABSTRACTS OF PREVIOUSLY REPORTED CASES.

I. MONOD (1827). Bull. Soc. anat. de Par., 1827, 2 ed. 1841, II, 192.

*Right lobar pneumonia; thrombosis of the right upper extremity 7 days after onset following venesection; subsequent septico-pyæmia; death on the 38th day of the disease.*

Male, aged 45. Pneumonia of the right upper and lower lobes. Three venesections (two in the right arm and one in the left). Following these a thrombosis of the vein opened in the right arm, at the elbow, was noted on the 7th day, with an abscess formation in this situation. The abscess was opened later as well as one on the dorsum of the left hand and one in front of the right patella. Bed sores followed. The patient grew progressively weaker and died on the 38th day of his disease and the 31st of the thrombosis.

At the autopsy the spinal meninges seemed somewhat discolored. The right upper lobe of the lung was entirely infiltrated with pus, while the lower lobe showed beginning hepatization. The heart was pale and flabby. There were patches of arteriosclerosis in the arteries. The superficial radial and ulnar veins contained ante-mortem thrombi. The cellular tissue in the lower region of the right forearm was infiltrated with pus. This focus of suppuration was covered by an area of ecchymosis which extended down nearly to the dorsum of the hand. The median cephalic, basilic and a small portion of the median vein were considerably thickened and resembled arteries. Their lumina were almost obliterated and contained some pus. The surrounding tissue was filled with pus. The basilic vein was filled by a solid clot, but in the cephalic the clot had broken down almost. The cephalic's branches going to the deltoid and to the scapulo-humeral articulation were filled with solid clots. The deltoid was raised by a vast focus of pus, which communicated with the shoulder

joint. Solid clots filled the axillary and subclavian veins. There were enormous abscesses in the axillary, subscapular, and subspinous regions. An abscess also existed on the dorsum of the left hand. The popliteal vein and its branches communicating with the abscess in the right leg, at the knee, contained some solid clots, as did also the left hypogastric vein and some of its branches. There was an abscess in the pelvis.

II. Metcalfe (1852). N. Y. Med. Times, 1853, II, 193.

*Right lobar pneumonia; thrombosis of left external iliac, femoral, and popliteal veins during convalescence; sudden death from pulmonary embolism (?) about 3 weeks later.*

Female, aged 27. Alcoholic history. Right lobar pneumonia. Four days after onset was regarded as convalescent. At this time she called attention to her left lower extremity which was found somewhat swollen and very painful when pressure was made over the course of the popliteal and femoral veins. These vessels had a hard cord-like feel on deep palpation. The treatment consisted of cathartics, leeches along the course of the painful vessels, and hot fomentations of hop poultices. The leg and thigh, however, continued to swell and the pain persisted until two weeks later, when an improvement was noted. This lasted for about 8 days and she was finally allowed to sit up. On the following day she suddenly became weak and faint; there was great restlessness; great oppression on breathing and violent pain in the cardiac region. Her death resulted from syncope 15 minutes later. At the autopsy the lower third of the right lung was found involved in a pneumonic process. There were old pleural adhesions on the two sides. The heart showed fatty degeneration. The left external iliac, femoral and popliteal veins were found to be filled throughout nearly their whole extent by firm, whitish, fibrinous coagula, in many places adherent to their walls.

III. Vulpian (1863). Groussin: Étude sur les embolies pulmonaries. Thèse de Paris, 1864, 16.

*Pneumonia of both lungs; thrombosis of the left femoral vein and right pulmonary artery during convalescence; sudden death from pulmonary embolism 3 weeks after onset of attack.*

Female, aged 80. Since her 39th year had had several attacks of acute articular rheumatism. When 52 had right-sided hemiplegia. It lasted a year and was accompanied by some difficulty in speech, which continued 8 months longer. Right and left lobar pneumonia. Favorable course. Three weeks later on attempting to get out of bed she suddenly fell back dead. At autopsy the vessels of the brain were found very much sclerosed. The whole middle, almost all the upper and part of the lower right lobe of the lung was in a state of gray hepatization. There were 2 small cavities in the upper lobe. The left lung was likewise solidified in its

upper half and very numerous little grayish tubercles were seen in the middle of this consolidation, placed at almost equal distances from one another. The heart showed nothing of especial interest. The aorta was considerably sclerosed and in some places showed beginning ulceration with a softening of the atheromatous deposits. In places the aorta thus weakened was slightly dilated. The iliac and femoral arteries were also calcified and sclerosed. The upper branch of the right pulmonary artery contained a clot, adherent to the vessel's walls. It was evidently of ancient formation. In the lower branch of this artery another clot was found of more recent origin. The left pulmonary artery contained a clot 6-8 cm. long. It was evidently more recent than the others and did not offer any adherence to the vessel's walls. In the left femoral vein an old blood clot was found, in great part decolorized and beginning to disintegrate. The mucous membrane of the stomach was injected at its greater curvature and here 2 or 3 small ulcerations were observed.

IV. Barbanceys (1868). Étude sur le coagulation du sang dans les veins. Thèse de Paris, 1870, 50.

*Left lobar pneumonia; thrombosis of the left femoral vein during the course of the disease; death.*

Male, aged 55. Alcoholic history. Two attacks of pleurisy on the left side 5 and 4 years previously. Left lobar pneumonia following exposure to cold. Progress satisfactory and the pneumonia seemed to be on the point of resolution, when the patient became delirious and died a few days later. According to his account he noticed his left leg was swollen at the time of onset of his illness. When he entered the hospital 10 days later thrombosis of the left femoral vein was made out. At autopsy the lower third of the left lung was found involved in an old pneumonic process, while the upper two-thirds were invaded by more recent foci. In the left ventricle 2 organizing blood clots were found of small size. The left femoral vein was obliterated by a thrombus and markedly distended for 10 cm. about this clot, which was adherent to the posterior wall near where the internal saphenous vein emptied into it.

V. Barbanceys (1868). Op cit.

*Left lobar pneumonia; thrombosis of the left femoral vein during convalescence; complete recovery.*

Male, aged 30. Alcoholic history and had been exposed to cold and rain before the attack. Left lobar pneumonia. Severe attack. Twelve days after onset his left lower leg suddenly became increased in size and he complained of a violent pain in the knee. On the following night this pain was felt in the calf of the leg and was so severe as to make him unable to bear the pressure of the bed clothes. The femoral vein could be palpated as a hard cord. The subcutaneous veins were more prominent than those in the right leg. After 9 weeks he made a complete recovery.

VI. Lancereaux (1861). Atlas d'anatomie pathologique, Paris, 1871, 168

*Left lobar pneumonia; thrombosis of the right and left femoral veins and left internal saphenous vein shortly after the crisis; sudden death from pulmonary embolism some days later.*

Female, aged 66. Left lobar pneumonia. Favorable course. Crisis on the 7th day. Shortly after this she complained of slight pain in the calf and slight œdema of the legs was noted. Some days later she got up out of bed in a fit of anger, walked about the ward, then got back into bed with great difficulty and expired a few minutes later. At the autopsy the left upper lobe showed a pneumonia undergoing resolution. The right pulmonary artery contained 2 blood clots entirely free; a 3d was found in the branch of this artery which goes to the lower lobe. This last appeared to be of an older formation than the other 2. There was firm œdema of both legs, localized in the left leg at its lower part, but affecting the entire right leg. The vena cava, external iliac, and hypogastric veins were free, but the right femoral was partially obliterated by a clot extending from the deep femoral upwards to Poupart's ligament. Below there was another clot, but less voluminous. The left internal saphenous was filled by a thrombus jutting out 1 cm. into the femoral vein and the deep femoral enclosed another which was also prolonged into the femoral for 2 cm.

VII. Hayem (1870). Comptes Rend. des Séances et Mém. de la Soc. de Biol., 1870; II, 5th ser., 161.

*Right lobar pneumonia; thrombosis of the right and left external saphenous veins, which was found at autopsy, after a sudden death from pulmonary embolism 5 days after the crisis.*

Female, aged 49. Right lobar pneumonia. Favorable course. Delayed crisis on the 22d day. Five days later she got up without permission, and then suddenly called for help. Shortly thereafter she was found in a syncopal state on the floor and died before a physician could come to her aid. At autopsy the right lung showed a pneumonia undergoing resolution. There were some old adhesions in the region of the right upper lobe and slight bloody serous effusion was noted on the right side. The left lung was emphysematous and congested. The mitral valve showed a slight thickening at its free border. In both pulmonary arteries clots were found of varying sizes. They were also present in the branches of these arteries. The spleen was enlarged and very soft. Some calcareous plaques were noted along the course of the aorta. In the lower extremities some superficial, non-inflammatory varices were found. In both external saphenous veins clots were found, which appeared to be from 8 to 15 days old.

VIII. Lande (1871). Mém. et bull. soc. méd. d'hôp. de Bordeaux, 1871, VI, 153.

*Right lobar pneumonia; during convalescence thrombosis of the right upper extremity; sudden death from pulmonary embolism.*

Male, age not given. Right lobar pneumonia of about 12 days duration. During convalescence (exact time not given) he complained of pain in his right arm, which had come on abruptly the preceding night. On examination a hard, painful, cord-like swelling was noted in the cephalic and median cephalic veins. A bandage was applied to the arm to almost completely immobilize it and absolute rest was enjoined on the patient. He did not heed this order, however, and on the 3d day, while endeavoring to raise himself in bed, he suddenly fell back dead. At autopsy the veins of the right arm were free and presented no traces of inflammation. A clot was found in the right pulmonary artery, which completely obliterated the left lower branch and both of its right branches. The clots were entirely free and easily removed.

IX. Hayem (1874). Troisier: Phlegmasia alba dolens. Thèse de Paris, 1880, 101.

*Right lobar pneumonia with pleurisy on both sides; thrombosis of both right and left internal saphenous veins during convalescence; recovery.*

Male, aged 24. Previous history of 2 attacks of acute articular rheumatism. Pneumonia of the right upper lobe with right-sided pleurisy and subsequent pleurisy of the left side. During convalescence, on the 4th day of normal temperature, he complained of sharp pain in the upper part of the left leg along the course of the internal saphenous vein, which later appeared as a hard cord-like swelling on palpation. A diffuse redness and an œdema of this extremity was also noted. Four days later the same findings were observed in the right leg. There was no rise of temperature at any time. Two weeks later pain was complained of at the umbilicus and shortly thereafter the superficial veins in the region of the right iliac fossa were found to be hard and painful on palpation. Complete recovery in 8 weeks.

X. Lepine's case (1878). Troisier: Phlegmasia alba dolens. Thèse de Paris, 1880, 99.

*Left lobar pneumonia; crisis on 10th day; thrombosis of left femoral vein 3 days later; recovery in 3 weeks.*

Male, aged 31. Pneumonia of the left lower lobe. Favorable course. Crisis on 10th day. Three days later patient complained of pain in abdomen which extended down into the left thigh, being especially located about Poupart's ligament. The thigh was swollen and hard to the feel. The surface temperature was elevated and there was some discoloration of the skin. Œdema of the foot and leg was observed, which yielded easily to

pressure and presented no points of resemblance to inflammatory œdema. The red blood corpuscles were reduced and numbered 3,800,000; the white blood corpuscles were 14,000. The swelling disappeared in 3 weeks. The treatment consisted in fixation of the leg and applications of a soothing ointment.

XI. Valette: Des coagulations veineuses dans la pneumonie et de leurs conséquences. Thèse de Paris, 1881, 4.

*Left lobar pneumonia; sudden death from pulmonary embolism during convalescence; at autopsy a thrombus was found at the bifurcation of the iliac veins, which presented no symptoms during life.*

Male, age not given. Left lobar pneumonia. It went on to a progressive but incomplete defervescence until 14 days after its onset, when the patient was suddenly seized with an attack of difficult breathing and shortly thereafter expired. At the autopsy some pleural adhesions were noted and partial consolidation of the whole left lung. The left pleura contained 120-150 ccm. of bloody serum. In the right pulmonary artery an enormous blood clot was found obliterating its entire lumen as well as its entire branches. The right lung was much congested. The right side of the heart contained a large clot, not adherent, and continuous with the clot in the pulmonary artery. At the bifurcation of the two iliac veins a blood clot was found. Its periphery of fibrin was a little discolored and its center was brownish red, as if the clot had been formed from the periphery. It is interesting to note that there were no symptoms before death indicating a thrombosis of the 2 iliac veins.

XII. Fabries (1887). La Sem Méd. 1888, VII, 144.

*Right lobar pneumonia; crisis on 12th day; thrombosis of the right femoral vein 2 days later, followed by thrombosis of the left femoral vein and symptoms of thrombosis in the kidneys, stomach, and left lung; recovery.*

Male, aged 19. Right lobar pneumonia. Favorable course. Crisis on the 12th day. Two days later thrombosis of the right femoral vein followed in 8 days by thrombosis of the left femoral vein. The swelling in these extremities gradually subsided and finally an indurated cord in the place of these veins was the only symptom left. About 3 weeks after the crisis, after a walk, he was suddenly seized with an attack of vomiting accompanied by other gastric disturbances. On the following day hæmaturia was observed and pain in the region of the right kidney and ureter was complained of. These latter symptoms vanished in 5 days, but reappeared 3 days later in the region of the left kidney. One week later the patient had an attack of profuse hæmatemesis and 3 bloody stools. This was followed in 14 days by pain in the left side and bloody sputum, "indicating that a clot had obliterated one of the branches of the left pulmonary vein." These various symptoms gradually subsided and the patient seems to have recovered.

XIII. Mya. Riv. gen. ital. di clin. med., 1891, III, 230.

*Left lobar pneumonia; thrombosis of the right femoral vein on the 2d day of the disease; death on the 3d day.*

Male, aged 67. Alcoholic history. Arterio-sclerosis quite marked. Left lobar pneumonia. On the 2d day of the disease there was œdema of the right lower extremity and tenderness on palpation below Poupart's ligament. From here to the lower angle of Scarpa's triangle there was marked cord-like induration. Death on the third day. At the autopsy there was found gray hepatization of the left lung with œdema of the right lung. There were infarcts of small volume in the lungs and the kidneys, and a condition of grave atheromatosis with aneurysmal dilatation of the ascending portion of the arch of the aorta. The aortic valves were much retracted and insufficient. They contained some vegetations. The right femoral vein, immediately below Poupart's ligament, contained a large reddish-gray thrombus of puriform aspect, strongly adherent to the vessel's intima. The thrombus was composed of many red blood corpuscles badly preserved, many white blood corpuscles, and some fibrin. It also showed numerous capsulated diplococci, which decolorized by Gram's method and were pathogenic to guinea pigs in 12 hours, if injected subcutaneously.

XIV. Mya (1891). Loc. cit.

*Left lobar pneumonia; thrombosis of the left femoral and internal saphenous veins during convalescence; recovery.*

Male, aged 58. Thirty-three years previously had an attack of lymphangitis of the left lower extremity, followed by a slight permanent swelling of that leg. Left lobar pneumonia. In 5 days resolution began when a new and grave exacerbation intervened. It was ushered in with pain in the side, dyspnœa, and bloody sputum. After 7 days, resolution commenced again. Some time during this period thrombosis of the left femoral vein with painful œdema of the left leg came on. The superficial veins were swollen and the internal saphenous was palpable as a firm hard cord. The temperature seems to have been subnormal even when the thrombosis was first noted. There was some poikilocytosis and the red blood corpuscles were reduced to 2,080,000, and the hæmoglobin was 35%. The swelling of the extremity was gradually reduced in size, but not to normal. The patient seems to have made a good recovery.

XV. Laache (1886). Deutsche med. Wchnschr., 1893, XIX, 785.

*Left lobar pneumonia; thrombosis of the right femoral vein 4 days after the crisis; recovery after several months.*

Male, aged 21. Pneumonia of the left lower lobe. Uneventful course. Four days after crisis the right lower extremity was swollen and, on examination, the femoral vein was found to be enlarged like a cord and very tender. Some of the glands in the right inguinal region were also enlarged and tender. After several months there was complete recovery.

XVI. Da Costa (1893). Am. J. Med. Assn., 1894, XXII, 173.

*Left lobar pneumonia; thrombosis of the right and left femoral veins during convalescence; slow recovery.*

Male, aged 34. An occasional drinker, but a constant user of tobacco. Severe attack of "la grippe" 6 six years before present illness; 2d attack 4 years later. A month prior to admission to hospital he had been treated for pleurisy at a Newark hospital. He was discharged from there after 4 weeks and returned to work. He found employment as a rigger, which exposed him to all kinds of weather. Pneumonia of left lower lobe. After 10 days, while convalescing, he complained of pain in the right leg. On examination there was tenderness on pressure, especially below the saphenous opening. It followed the course of the vein. On the following day the leg was swollen to nearly twice the size of the left and the veins seemed much distended. There was some distension of the abdominal veins, especially on the left side. To the touch the leg was cold and the femoral vein could be palpated. It was extremely hard and tender. The swelling and cord-like condition of the veins of the right leg gradually subsided, but during the 4th week, after admission to the hospital, the left leg became swollen. The veins in the upper part of the thigh were considerably distended and the surface veins around the saphenous opening were quite prominent. There was pain and tenderness on pressure in the thigh and marked sensitiveness in Scarpa's triangle. Pitting was obtained on pressure as well as some slight tenderness over the femoral vein. He made a slow but complete recovery. The treatment consisted in the elevation of the leg and hot, moist applications, first poultices and then warm fluid extract of hamamelis. It is interesting to note that there was no elevation of temperature at the time of the thrombosis and that the heart's action was feeble.

XVII. Nourse. Med. Record, 1894, XLV, 525.

*Left lobar pneumonia; thrombosis of left internal saphenous during convalescence; recovery in 3 weeks.*

Female, aged 32. Phlegmasia alba dolens after 1 pregnancy and a troublesome varicose vein after another. Ill with "la grippe" 1 week before onset of present illness. Left lobar pneumonia complicated by considerable pleurisy. Slow convalescence. Finally after sitting up for a couple of hours and walking about, the left leg began to swell and became exceedingly painful and tender to the touch. A swelling was then made out over the internal saphenous vein, an inch below the saphenous opening and a similar bunch was noted in the groin above Poupart's ligament. They were very tender when felt. Ultimately the saphenous vein was palpable as a hard, round cord. The leg was considerably swollen, especially below the knee. Under treatment this subsided in 3 weeks though the induration and occlusion of the vein persisted. The treatment consisted in rest, opium internally to relieve the pain, belladonna plasters over the swelling and hot fomentations to the entire leg.

XVIII. Hasell. Ontario Med. J., 1894, II, 197.

*Right lobar pneumonia; crisis on 9th day; 5 days later thrombosis of left saphenous vein; gradual recovery.*

Male aged 19. Had an attack of appendicitis 15 days previously which subsided in 2 days. This was followed by right lobar pneumonia complicated by pleurisy and probably caused by exposure on his recovery from appendicitis. Favorable course. Crisis on 9th day. Five days later was seized with a sudden pain in his left thigh and leg. They then began to swell and became exceedingly tender; the pain was along the course of the saphenous vein, which had evidently become inflamed. The temperature rose again to 101° and was still above normal when the case was reported, though the pain and swelling had much subsided.

XIX. Porte. Dauphine Méd., 1894, XVIII, 108. Also La méd. moderne, 1894, V, 826.

*Right lobar pneumonia; 6 days after crisis thrombosis in right leg; death 3 days later.*

Female, aged 48. Pneumonia of right apex. On the 6th day of apyrexia phlebitis of right leg. Three days later dyspnœa, pain in the side, fainting spells, rapid irregular pulse, high temperature and death. At autopsy red hepatization of the right lung was found with marked congestion at the base of the left lower lobe. A branch of the pulmonary artery on this side was obliterated by a voluminous clot occupying a length of 4-5 cm. There was a polypus-like clot on the tricuspid valve. The right internal saphenous vein was obliterated by a thrombus, but the femoral vein was free.

XX. Jones (1895). Nursing Record, 1896, XVI, 271.

*Right lobar pneumonia; thrombosis of both lower extremities during convalescence; endocarditis; recovery.*

Male, aged 32. Right lobar pneumonia complicated by pleurisy. Three weeks after its onset was convalescing and was returning to bed, when he found he was unable to use his left leg and complained of acute pain running from the groin to the knee. Later the leg became very painful and began to swell. The pain and tenderness finally went to the left foot and was diagnosed by a physician as due to periostitis of the metatarsal bones. Three weeks after the onset of symptoms in the left leg, pain was complained of in the right foot and along the course of the femur. This was diagnosed as femoral phlebitis and periostitis of the femur. The day following the patient was suddenly seized with an attack of labored breathing and gasped for breath. The pulse was now noted to be feeble and thready. Some hours later marked endocarditis was found on cardiac examination. This gradually cleared up and the pain and swelling of the extremities subsided in 3 months time. The treatment consisted in hot spongiopilene fomentations and belladonna liniment, with internal treatment for the pain. Later a light bandage and an elastic stocking was employed.

XXI-XXVII. Dickinson. Brit. M. J., 1896, I, 149.

Dickinson states he has seen 7 cases of peripheral venous thrombosis in pneumonia, 4 were in young women and 2 of these were chlorotic. These 7 cases are given in Dr. Welch's list so I insert them in this series, though the mention of them is very brief and unsatisfactory.

XXVIII. Katz (1897). Deutsche med. Wchnschr., 1897, XXIII, 436.

*Left lobar pneumonia; crisis on 7th day; about noon of that day thrombosis of left lower extremity; complete recovery in 3 months.*

Male, aged 37. Slight alcoholic history. Left lobar pneumonia. Favorable course. Crisis on 7th day. About noon of that day he was suddenly awakened by a violent pain in his left leg, which he observed was much swollen. The entire leg was markedly œdematous on the physician's visit shortly after this and was slightly cyanotic. The femoral vein was not palpable on account of the œdema. The patient complained of feeling cold and of tension in the entire limb. Elevation of the leg and rest in bed for 3 months enabled him to work again.

XXIX. Da Costa (1898). Phila. Med. J., 1898, II, 579.

*Left lobar pneumonia; during convalescence thrombosis of both lower extremities; recovery in 4 weeks.*

Female, aged 19. Pneumonia left lower lobe complicated by pleurisy. Termination by lysis. While convalescing complained of pain in the calf of the right leg, which was distinctly swollen and painful on palpation. There was tenderness along the course of the long saphenous vein, but no sign of redness or resistance. The temperature now rose from 100.2° to 103°. The next day the left leg and thigh were also swollen and mottled. There was considerable tenderness in the calf. The swelling was firm and not œdematous; nor were the veins especially prominent, though engorgement of the external saphenous near its passage into the popliteal vein was observed. Under treatment the pain in the legs subsided in 4 weeks, though there was still some soreness in the calves elicited by pressure at the end of this time. The treatment consisted in the elevation of the legs and application of lead water and laudanum. The lung did not clear up entirely and at the angle of the scapula there were signs of a cavity formation. In the 6th week after admission tubercle bacilli were found in the sputum.

XXX. Da Costa (1898). Loc. cit.

*Left lobar pneumonia; termination by lysis; 2 days later thrombosis of the left lower extremity; recovery.*

Female, aged 28. Pneumonia of the left lower lobe. Termination by lysis. Two days after the lungs were clear and normal she complained of pain and weakness of the left leg on trying to walk. On examination no swelling and no enlargement of the veins was made out, but there was tenderness in the calf. Within a few days the temperature rose to

101°, and the thigh and leg became painful and swollen, the swelling being principally about the knee. A mottling of the surface was observed with a prominence of the veins. On palpation the femoral vein was hard and swollen. The swelling and pain subsided after a week's treatment. The treatment consisted in the elevation of the leg, applications of witch hazel, and then of lead water and laudanum, and an occasional saline laxative.

XXXI. Gauchet. De la phlébite dans la pneumonie. Thèse de Nancy, 1900, 70.

*Right lobar pneumonia; thrombosis of the right internal saphenous vein on the day following the crisis; gradual recovery.*

Male, aged 52. Pneumonia of the right upper lobe. Favorable course. Crisis on the 9th day. The day following he complained of pain in the lower right leg, inner portion. An examination revealed quite marked varicose veins of both lower extremities and a mottling was observed extending from the right internal malleolus upwards to about the middle and inner third of the leg. This was more marked on its anterior aspect. On palpation in this region a superficial vein was found to be thrombosed for a distance of about 5 cm. The lower part of the internal saphenous could be well felt. It was quite painful to the touch. No rise of temperature was recorded with the onset of this sequela and no œdema of the leg was detected except when the patient was up and about. He seems to have made an uneventful recovery.

XXXII. Hall. Phila. Med. J., 1901, VIII, 791.

*Pneumonia of both lungs; thrombosis of the left leg on the 9th day of the disease and of the right leg 16 days later; gradual recovery.*

Male, aged 25. Pneumonia of the whole right lung and left lower lobe with pleural and pleuro-pericardial friction rubs. Severe infection. Thrombosis of left leg on the 9th day (veins not stated), followed 16 days later by thrombosis of the right leg. It is not noted whether the thrombosis occurred during the course of the disease or during convalescence. It seems probable from the history that the left leg might have been involved during the course of the disease. Gradual recovery.

XXXIII. Clarke. Brit. Med. J., 1901, II, 764.

*Lobar pneumonia; 9 days after its onset thrombosis of one upper extremity; death.*

Sex and age not given. Pneumonia (side not stated). Nine days after its onset thrombosis of the veins at the bend of the elbow and part way down the forearm set in with a rigor. The leucocytes numbered 20,000 and pneumococci were found in the blood. Three injections of antipneumococcic serum were given without effect. Death. At the autopsy the thrombi were found in the veins indicated and septic infarcts were observed in the spleen and the lungs.

XXXIV-XLIII. Sears and Larrabee. Med. and Surg. Reports Boston City Hospital, 1901, XXI, 16.

Out of 949 cases of pneumonia treated at the Boston City Hospital peripheral venous thrombosis "was found in but 10 cases, 5 of whom were men. It came on late in the course of the disease, 5 to 14 days after the fall of temperature, with the exception of the only fatal case, in which the affected right upper lobe suppurated and death took place on the 14th day. The cases in which it occurred rather exceeded the average length, as in but 2 had the temperature reached normal in less than 10 days, while in 1 it ran 18 and in another 24 days. The left leg was the favorite site in the ratio of 6 to 3. In one case it was double. The symptoms were never severe."

XLIV. Monmeneu (1898). Rev. de med. y cirurg. pract., Madrid, 1902, LVII, 321.

*Left lobar pneumonia; thrombosis of the veins of the lower extremities during the course of the disease; gradual recovery.*

Female, aged 32. Left lobar pneumonia. On the 7th day of the disease, when the left lung was completely solid, the temperature went up to 102.5° and the patient complained of an acute pain in the left leg, especially in the popliteal region. On examination the entire left leg was œdematous and quite hard and tense on palpation. Fifteen days later, when the œdema of the left leg was subsiding and the pain diminishing, similar symptoms were observed in the other lower extremity. The patient was discharged 3 months after the onset of her illness. The recovery was not complete as an œdema of the lower extremities would occur after exercise. The treatment consisted in rest, immobilization of both lower extremities, with the application of cotton and hot fomentations.

XLV. Obrecht (1901). Phlegmasia alba dolens dans la pneumonie. Thèse de Nantes, 1902, 50.

*Right lobar pneumonia; thrombosis of the right axillary vein during the course of the disease; gradual recovery.*

Female, aged 58. Right lobar pneumonia. During the course of the disease, 9 days after the onset, the patient complained of pain in the right arm. On examination the fingers and hand of this arm seemed very œdematous and were painful on pressure, the skin was not reddened. Shortly thereafter the œdema became hard and tense in character, and the axillary vein palpable, rolling readily as a hard cord under the finger. Subsequently a soft œdema of the lower extremities developed, but it was not accompanied by a venous thrombosis. The arm was immobilized and 4 weeks later all signs of a venous thrombosis had disappeared. The patient was discharged 6 weeks thereafter.

XLVI. Coleman. Trans. Am. Climat. Assn., Phila., 1903, XIX, 161.

*Right lobar pneumonia; thrombosis of the veins of both lower extremities during convalescence; recovery.*

Male, aged 17. Pneumonia of the right upper and lower lobes. Crisis on the 12th day. Four days later the left leg began to swell, but in a week the swelling subsided and the leg appeared normal. About 4 days later the right leg then began to enlarge and became very sensitive on palpation. Under immobilization with cotton and supporting treatment this leg returned to normal, as the other, in a week. Patient had completely recovered on discharge.

XLVII. Widal, Lemière and Gadaud. Bull. et. mém. de la Soc. méd. des. hôp. de Paris, 1903.

*Right lobar pneumonia; thrombosis of the left popliteal vein during convalescence; recovery.*

Male, aged 39. Pneumonia of the right apex. Favorable course. Temperature fell by lysis, reaching normal on the 9th day of the disease. Five days later the patient complained of a sharp pain in the left calf. On examination a thrombosis of the left popliteal vein was made out. The affected vein was varicosed. The left leg was then immobilized for 3 weeks, at the end of which time the patient left the hospital, having made a complete recovery. By blood culture made on the 7th day of the disease, the pneumococcus was recovered.

XLVIII. Miller. Phila. Med. J., 1903, 191.

*Right lobar pneumonia; thrombosis of the left femoral, internal saphenous, popliteal and superficial veins during convalescence; recovery.*

Male, aged 41. Right lobar pneumonia. Favorable course. Temperature fell by lysis, normal on the 16th day. Thirty-six hours later, on the 18th day, the patient complained of pain in his left calf, which was found on examination to be exquisitely sensitive and 3 cm. larger than the right. There was tenderness over the femoral and the upper part of the internal saphenous veins, in the popliteal space, and on the calf. All the superficial veins of the affected leg were enlarged and there was slight œdema over the lower third of the tibia and about the ankle. Coincident with the swelling of the leg, the temperature rose to 101.4°. "There was no leucocytosis, and the blood culture, taken from a branch of the internal saphenous over the instep, on the 3d day of the thrombosis, proved negative." On the 23d day of the thrombosis, the patient was discharged at his own request, though the affected leg was still enlarged and somewhat stiff.

XLIX. Persons. Trans. Lucerne Co. Med. Soc., Wilkesbarre, 1904, XII, 102.

*Right lobar pneumonia; thrombosis of the veins in one lower extremity during convalescence; recovery.*

Female, aged 28. Pneumonia of the right lower and middle lobes. Favorable course. Termination by crisis on the 8th day. On the 14th day peripheral venous thrombosis of one leg (side not stated) was noted. It ran its course in 4 weeks, terminating in complete recovery.

The other example Persons cites occurred in a case of broncho-pneumonia.

L. Pierre. Contribution à l'étude de la phlébite pneumonique. Thèse de Paris, 1904, 18.

*Right lobar pneumonia; pneumococcus empyema starting seven days after the onset of the disease, followed by an operation for the same; peripheral venous thrombus of the left lower extremity, first noted 21 days after the beginning of the disease; slow recovery.*

Woman, aged 33. Pneumonia of right lung at the base. Subsequent appearance of a pneumococcus infection of the right pleura which necessitated an operation later. It was first noted 7 days after the onset of the pneumonia, but was not found to be purulent until 16 days later. Twenty-one days after the patient's illness began, she complained of a sudden, sharp pain in the left lower extremity, which on examination presented a hard and painful œdema. During the course of the disease the patient had a severe attack of cardiac weakness. The affected leg was immobilized and the patient was progressing towards a slow recovery when the author's thesis was published.

LI. Gaultier. Bull. de la Soc. anat. de Paris, 1904, 79, 565. Also Pierre, op. cit., 22.

*Left lobar pneumonia; sudden death from pulmonary embolism on the 7th day; at the autopsy a thrombosis was found in the left femoral vein, which was varicosed.*

Male, aged 35. Alcoholic history. Pneumonia of the left apex. Crisis on the 6th day. On the day following, complained of pain in the left calf, but nothing was found on superficial examination. In the evening he got out of bed without permission, and while attempting to return to bed, suddenly fell backwards and died five minutes later of asphyxia. At the autopsy, on the following day, the upper part of the left lung was found in a state of hepatization. The right pulmonary artery contained a large non-adherent fibrinous clot, which extended into the inferior branch of this artery. The vena cava, common iliac, hypogastric, and external iliac veins were free, but the left femoral vein was varicosed and presented, in part of its course, a clot which extended to the crural arch.

## General Considerations on Peripheral Venous Thrombosis in Pneumonia.

The number of cases presented is small and conclusions drawn from such a list are, of necessity, somewhat uncertain. Yet we venture to give the following facts which we have found from a study of our 3 cases and the table of those previously reported:

I. The infrequency of thrombosis in pneumonia should be noted. It was only possible to collect 54 cases. This is a matter of surprise, possibly, for pneumonia is a disease in which the blood is especially rich in the elements that are necessary for clotting. The condition, however, is not as rare as the published cases would lead us to suppose. I have heard of a number of unpublished cases since this article was first written. Among them is one related by Dr. G. Jarvis Bowens, of Norfolk, Va., in a personal communication to Dr. Osler, where the patient had, during convalescence from a right lobar pneumonia, a thrombosis of some of the veins of the right arm. He later made a complete recovery. Preble (23) states that he has seen 2 examples of thrombosis of the upper extremity in pneumonia. The statistics of Smith, Ashton and Landis, Norris, Sears and Larrabee, and our own may give us some idea as to its frequency. For example, Smith (24) noted it 3 times among 488 cases of pneumonia treated at the Presbyterian Hospital in New York (.61%); Ashton and Landis (25) found it once in 991 cases treated at the Philadelphia General Hospital (.10%); Norris (26) records it twice in 500 cases treated at the Pennsylvania Hospital (.40%); and Sears and Larrabee (27) have observed it 10 times in 949 cases treated at the Boston City Hospital (1.05%). It has only been seen in the 3 instances, related above, in 558 cases treated at the Johns Hopkins Hospital (.46%). Haward (28) states he has found but 1 case of venous thrombosis due to pneumonia out of 2903 necropsies.

II. In 35 out of the 44 cases which are reported fairly in detail the thrombosis occurred during convalescence, in 1 on the day of the crisis, and in 8 during the course of the disease. It must, consequently, be generally regarded as a sequela and not as a complication of pneumonia.

III. The lower extremities were generally involved. I can find but 5 cases reported where there was thrombosis elsewhere. In 4 of these it was in some of the veins of one upper extremity. The 5th case, also, showed a clot in the right pulmonary artery. In the case of Ashton

and Landis, which resulted fatally, the thrombosis was in the external jugular and axillary veins. There was a case admitted to the Johns Hopkins Hospital (Hospital No. 21,367), where a thrombosis of the left jugular vein was detected, a day before death, in an old man aged 84, whose heart's action was feeble, who had quite marked arteriosclerosis and who presented some doubtful signs of pneumonia. No autopsy was obtainable, so I have not included the case in this group.

As in typhoid and other infectious diseases, so here we find the thrombi mostly in the left femoral vein. This was involved alone in 8 cases, the left femoral and internal saphenous in 1; the left internal saphenous in 2; the left femoral, internal saphenous, popliteal, and superficial veins in 1; the left external iliac, femoral and internal saphenous in 1; the left popliteal in 1; the right femoral in 2; the right and left femoral and left internal saphenous in 1; the right internal saphenous in 2; the right popliteal in 2; both femorals in 6; both internal saphenous and superficial abdominal veins in 1; both external saphenous veins in 1; and the common iliacs at their bifurcation in 1. Adding to these the cases where the extremities but not the vein involved are given, we find that the left extremity alone was concerned in 20 cases, the right in 10 and both extremities in 11. The greater frequency of venous thrombosis in the left leg than in the right is attributable to the more difficult return flow from the former in consequence of the greater length and obliquity of the left common iliac vein and its passage beneath the right common iliac artery. It has also been suggested that pressure upon this vein by a distended sigmoid flexure or rectum may likewise contribute to slowing of the blood current upon this side (29).

The upper extremities were implicated, as has already been mentioned, 4 times, the veins affected being distributed as follows: the right axillary vein alone in 1 case; the right axillary with the subclavian in 1; the right cephalic and median cephalic in 1; and the veins of the elbow and part way down the arm (side not given) in 1. In the second case (Monod's), venesection which was thrice resorted to, was undoubtedly an important cause of the thrombosis, from the traumatism it set up in the walls of the veins.

*Etiology.*—It is stated that thrombosis in pneumonia is seen occasionally in protracted cases (30). From the above list 29 can be properly so-called, while 15 were light cases, varying, when their crises were given, from 7 to 9 days. Six terminated by lysis.

*Sex.*—Males seem somewhat more liable than females. Our list includes 32 males and 21 females.

*Age.*—Although arteriosclerosis may be a predisposing factor, yet thrombosis has been mostly met with in those approaching middle life. There were no cases reported in the first decade of life; between ten and twenty 4; between twenty and thirty 9; between thirty and forty 9; between forty and fifty 4; between fifty and sixty 4; between sixty and seventy 3; between seventy and eighty 1.

Da Costa (31) thinks feeble circulation and altered blood condition are factors which play an important part. The former might result from obstruction to the blood flow, and, as examples of this, the following cases may be cited: Case II, right-sided hemiplegia 28 years previously; Case X, lymphangitis of the left lower extremity 23 years before the pneumonic attack; Case IX, marked arteriosclerosis; Case XIII, phlegmasia alba dolens and varicose veins during previous pregnancies; and our second case, which presented a feeble heart, arteriosclerosis, marked varicose veins and 43 years previously had had hemiplegia. Cases VII, XLVII, L, and LI also had marked varicose veins. The altered blood condition may be due to a great increase in fibrin elements and blood platelets in pneumonia, or it may be caused by the destruction of the red blood corpuscles. This was seen in Lepine's case, where the red blood corpuscles were reduced to 3,800,000; in Mya's case, where they numbered 2,080,000, and in our second case, where they amounted to 3,996,000. A prolonged course of fever and a profound toxæmia must also influence the blood condition even more greatly.

Yet the above factors, though conducive to thrombus formation, do not wholly explain it. They are predisposing in character and are frequently found where no thrombosis is observed. Consequently Da Costa suggests a primary infective phlebitis as the cause. Mya (32), however, who has made observations on the presence of pneumococci in thrombi resents this view and thinks these bacteria are found in this situation as it is an excellent culture medium. Gaultier (33), on the other hand, who obtained the pneumococcus from his case when it came to autopsy, considers the cause of the thrombosis to be a septicæmia due to a pneumococcus of attenuated virulence. He thinks this germ will be found in the walls of the affected veins, as well as at the borders of and within the clot. He calls attention to the fact that we must surmise some previous alteration in the walls of the implicated

veins before the onset of the thrombosis. (See Cases VII, XIII, XVII, XLVII, L, and LI in the List and our second case.) In our second case the cultures from the thrombus and from the blood were negative for pneumococci or any bacteria. This was likewise the result in our third case, but Widal (34) was later able, by a different method, to grow the pneumococcus from a blood culture he made in his case. Unfortunately no one has examined the thrombosed veins in pneumonia to find a diseased vessel wall as Kuskow (35) did in influenza. It seems probable that a previous infective phlebitis is the cause of the thrombosis, just as it is in typhoid and other infectious diseases, but it should be remembered that the bacteria found in other diseases are more frequently secondary invaders than the specific microorganism of the disease (36).

*Morbid Anatomy.*—It is unfortunate that thrombosis in this disease has not been well studied pathologically. When the cases have come to autopsy the observations have been mostly macroscopic in character. With the exception of Barbanceys (37), who made a slight and unimportant microscopic study of the thrombi in his case, Mya and Gaultier are the only observers who have done work in this line. Mya found the thrombus made up of many red blood corpuscles badly preserved, many white blood corpuscles and fibrin. A smear from the thrombus showed numerous capsulated diplococci, not decolorized by Gram's method. By inoculating a small quantity of the emulsion of the thrombus into a guinea pig, death ensued in 12 hours and a pure culture of the diplococcus of Fraenkel was obtained from the tissues. As the vessel wall was torn on scraping away the thrombus, a histological examination of the same was rendered impossible. Gaultier found the thrombus contained in his case encapsulated diplococci, which did not decolorize by Gram's method. They were situated in the midst of altered endothelial cells, deformed red blood corpuscles and many white blood corpuscles. Some of the white blood corpuscles seemed normal, while others showed extensive fatty degeneration. All of these cells were surrounded by fibrin in the process of a granular disintegration. A smear from the endothelial lining of the implicated vein, near the clot, also showed the presence of encapsulated diplococci, which did not decolorize by Gram's method. Unfortunately permission for the removal of a small piece of the affected vein, for microscopic study was not obtained.

The left lung was alone involved in 16 cases, the right in 17, and both lungs in 3. In 13 cases the extremity on the same side as the lung lesion was concerned. It was on the opposite side in eight.

*Symptoms.*—In those dying shortly after the formation of the thrombus no plegmasia alba dolens was observed, but it was noted in almost all the other cases. The symptoms have been well given by Da Costa (38) in the following words: "Slight rise of temperature, with occasional chilly sensations, and a sense of weight and stiffness and pain in the leg, sometimes very severe, are its early manifestations. The leg becomes sensitive, and is very painful on any attempted motion; the tenderness often shows itself first on pressing the calf. The swollen limb is white or mottled and has a hard but elastic feel; it does not pit on pressure, or pits but slightly; the femoral and internal saphenous veins are prone to be prominent, but may not be tender or manifestly altered. The disease gradually subsides; but aching, some numbness, stiffness, and want of control over the affected leg may remain for a considerable period and, with pain and swelling are likely to return on undue exertion."

In 21 of the above cases pain is spoken of as an initial symptom, and in 8 a rise of temperature is recorded.

*Prognosis.*—Of the 54 cases death occurred in 14, and 33 recovered. No definite information is given of 7. All but 1 of those that died came to autopsy, and in 8 death was due to a pulmonary embolism.

*Treatment.*—The treatment has been well given by Welch and Da Costa in their articles and needs only a few words here. Absolute rest in bed should be enjoined on all the patients for a length of time, depending on the severity of the case. This is of the utmost importance for in 2 of the above cases death was due to needless and unnecessary agitation. The possible sudden termination of such cases should always be kept in mind. Welch says it is a general rule that the patient should not be allowed to walk in less than 40 days.

The leg should be immobilized and hot fomentations of the lead and opium lotion, witch hazel, or laudanum may be employed to reduce the swelling and relieve the pain. Digitalis or other cardiac tonics may be given if necessary, and an occasional laxative is useful to prevent venous engorgement. "The mechanical support of a bandage or a long elastic stocking is later most advantageous." The period of disability varies for the cases in which it is given from 3 weeks to 3 months.

References.

1. Da Costa. Remarks on Clinical Cases. J. Am. Med. Ass., 1894, XXII, 173.
2. Da Costa. On Phlegmasia Alba Dolens or Phlebitis of the Leg in Pneumonia. Phila. Med. J., 1898, II, 519.
3. Welch. Thrombosis. Allbutt's System of Medicine, 1899, VI, 194.
4. Monod. Pneumonie compliquée de phlébite. Bull Soc. anat. de Paris, 1827, 2 ed., 1844, II, 192.
5. Valette. Des coagulations veineuses dans la pneumonie et de leurs consequences. Thèse de Paris, 1881, 45.
6. Hayem. Comptes Rend. des Séances et Mém. de la Soc. de Biol., 1870, II sér., 161.
7. Hayem. Troisier, Phlegmasia alba dolens. Thèse de Paris, 1880, 101.
8. Lande. Pneumonie; thrombose, mort subite par embolie. Mém. et Bull. Soc. med.-chir. de hôp. de Bordeaux, 1871, II, 153.
9. Jones. Notes on a Case of Phlebitis following Pneumonia. Nursing Record, 1896, XVI, 271.
10. Clarke. Discussion on the Pathology of the Pneumococcus Infection. Brit. Med. J., 1901, II, 764.
11. Hull. Report of Seventy Cases of Acute Lobar Pneumonia. Phila. Med. J., 1901, VIII, 791.
12. Gauchet. De la phlébite dans la pneumonie. Thèse de Nancy, 1900, 75.
13. Sears and Larrabee. An Analysis of Nine Hundred and Forty-nine Cases of Pneumonia. Med. and Surg. Reports, Boston City Hospital, 1901, XII, 16.
14. Monmeneu. Flebitis neumonica. Rev. d. med. y cirurg. pract., Madrid, 1902, LVII, 321.
15. Albrecht. Phlegmasia alba dolens dans la pneumonia. Thèse de Nantes, 1902, 70.
16. Widal, Lemière, and Gadaud. Recherche du pneumocoque dans le sang des pneumoniques. Bull. et Mém. de la Soc. méd. de l'hôp. de Paris, 1903, 3 ser., XX, 416.
17. Coleman. Some Complications of Pneumonia, with Report of Cases. Tr. Am. Climat. Ass., Phila., 1903, XIX, 161.

18. Miller. A Case of Femoral Thrombosis in Acute Croupous Pneumonia. Phila. Med. J., 1903, XI, 191.
19. Person. Two Cases of Phlegmasia Alba Dolens following Pneumonia. W. Luzerne Co. Med. Soc., Wilkesbarre, 1904, XII, 102.
20. Pierre. Contribution a l'étude de la phlébite pneumonique. Thèse de Paris, 1904, 68.
21. Gaultier. Étude sur la phlébite pneumonique à propos d'un cas terminé par embolie de l'artère pulmonaire. Bull. Soc. anat. de Par., 1904, 79, 565. (See also Pierre: op. cit.)
22. Osler. Practice of Medicine. New York, 1905, 6th ed., 182.
23. Preble. Pneumonia and Pneumococcus Infections. Chicago, 1905, 140.
24. Smith. Twentieth Century Practice of Medicine, New York, 1899, XVI, 69.
25. Ashton and Landis. Croupous Pneumonia. An analysis from clinical observations of 991 cases occurring in the Philadelphia General Hospital from May 1, 1897, to October 1, 1904. Am. J. M. Sc., 1905, CXXIX, 952.
26. Norris. Croupous Pneumonia. A clinical study of 500 cases from the present records of the Pennsylvania Hospital. Am. J. Med. Sc., 1901, CXXI, 684. (These 2 cases are described in Da Costa's second article,—q. v.)
27. Sears and Larrabee. Op. cit.
28. Haward. Phlebitis and Thrombosis. New York, 1906, 51.
29. Welch. Op. cit.
30. Osler. Op. cit.
31. Da Costa. Op. cit.
32. Mya. La trombosi venosa nell'infezione pneumonica. Riv. gen. ital. di clin. med., 1891, III, 230.
33. Gaultier. Op. cit.
34. Widal. Op. cit.
35. Kuskow. Zur pathologischen Anatomie der Grippe. Virchow's Arch., 1895, VXXXIX, 406.
36. Welch. Op. cit.
37. Barbancias. Étude sur la coagulation du sang dans [illegible]. Thèse de Paris, 1870, 136.
38. Da Costa. Op. cit.

# PNEUMOCOCCIC ARTHRITIS.

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Among the 658 cases of infection with Fraenkel's pneumococcus that have occurred during the past seventeen years[1] in the wards of the Johns Hopkins Hospital, the joints have been involved in 5. Of these 5 cases there were 2 of acute lobar pneumonia (Med. Nos. 5952 and 13,028) with a complicating arthritis, but which owing to the absence of bacteriological data are omitted from this series. Of the 3 remaining cases, 2 were reported by Cole (1) in 1902, and one by the author (2) in 1903.

The histories of these 3 cases are as follows:

CASE I. *Clinical Summary.*—Acute lobar pneumonia (?) (both apices): Arthritis of left ankle (12th day); arthrotomy (20th day); acute endocarditis(??); recovery.

Male, colored, aged 50, Med. No. 11,166; admitted April 9, 1900, in a semicomatose condition. Onset of illness had been sudden 10 days before with fever, delirium, and cough. The condition had grown gradually worse up to time of admission. For 5 days there had been jaundice.

On admission the patient appeared as though suffering from some acute infection. There were some signs of involvement of the apex of the right lung, but they were not definitely those of consolidation. The sputum was scanty and muco-purulent. Leukocytes, 15,000. Two days later the breath sounds at both apices had a slight tubular modification and there was impairment of the percussion note in both interscapular spaces. On this day the *left ankle* first appeared red and swollen and was painful on motion and pressure. The surface temperature over it was elevated. The sputum was very tenacious, muco-purulent, greenish-yellow, not bloody. The temperature continued elevated between 100° and 103.5°. On the tenth day after admission the ankle-joint was punctured and a syringe full of yellowish, purulent, blood-tinged fluid removed. This fluid contained numerous pus-cells and red blood-corpuscles, and many diplococci. Cultures made from this purulent fluid showed that these organisms were pneumococci. *Arthrotomy* was performed and the patient's condition at once began to improve, the temperature not becoming normal, however, until May 15—36 days after admission. The patient was discharged June 12. The ankle was still swollen, but the incision had healed.

[1] The manuscript was received in November, 1906.

That this patient certainly had a lobar pneumonia was impossible to say. Unfortunately no blood cultures were taken. During the illness a systolic murmur developed at the apex decreasing much in intensity, however, before the patient was discharged. From the history and signs the probability is that a lobar pneumonia occurred and that the arthritis and endocarditis (?) were secondary manifestations of a general infection.

Case II. *Clinical Summary.*—Previous arthritis deformans; acute arthritis of both knees; meningitis; secondary broncho-pneumonia; suppurative nephritis; death.

Murray, colored, aged 55, married, Med. No. 12,547. His occupation was that of an "oyster shucker." He was admitted to the Johns Hopkins Hospital during the evening of February 13, 1901, complaining of pain in his joints. He was in a peculiar mental state; appeared dull and answered questions in a very vague, rambling, inaccurate manner, so that no definite history could be obtained. On the next day the following notes were obtained from his wife.

He had apparently been a fairly healthy man; there was no history of any former acute illnesses. For several years he had had attacks of pain and swelling in the joints. These attacks were evidently not very severe, as they had not confined him to bed. The exact duration of these attacks, and which joints were involved, could not be learned. For four or five weeks before admission, however, both knee-joints had been swollen, the right more than the left. They had been somewhat painful, and he had been lame in consequence but had not been confined to bed. On February 10, three days before admission, he had a slight chill in the afternoon and another during the night. He did not appear very ill the next day, but remained at home. On the following day (the day previous to admission) he appeared worse, and complained of pain in the lower left axilla and at the apex of the right axilla. During the night he appeared feverish and at times was delirious. This condition lasted during the following day up to the time of admission. At no time had there been any cough, expectoration, or dyspnœa.

Examination on admission showed the patient to be poorly nourished. He was complaining of intense pain in his knees and ankles. His mental condition was peculiar, his answers to questions were very vague and inaccurate. The temperature was 99.8°, pulse 96, respirations 24. There was no stiffness of the neck or retraction of the head, no dyspnœa or cyanosis, no herpes on lips. The tongue was heavily coated with a white fur, the lips and mucous membranes were pale. Examination of the chest showed a slight impairment of the percussion note in the left infraclavicular space. The breath sounds were everywhere rather feeble, and over the lower back on both sides there were heard a few moist râles. Nowhere were the breath sounds tubular in quality. The heart sounds were irregu-

lar and weak. The pulse was of small volume, low tension and irregular. Both knees and ankles were swollen, hot, and red. There was a considerable accumulation of fluid in and about all these articulations. At 11 a. m. on the following morning this note was made by Dr. Osler:

"The patient is completely apathetic; he does not respond to questions. The pupils are equal and equally contracted; the head is turned a little to the left. Movements on the two sides of the face are equal. The wrists, ankles, and knees are swollen. The right knee is more swollen than the left, and the capsule is tense and contains fluid. The patient winces when the joints are touched. There is no general cutaneous or muscular hyperesthesia. Patient can be lifted by his head without bending the neck."

Kernig's sign was not tested for on account of the pain on motion. The knee-jerks could not be elicited. The temperature had risen during the night, and at 10 a. m. reached 105°. The signs of pulmonary involvement were no more definite than on admission.

*Blood Examination.*—Red blood-corpuscles, 3,650,000; leukocytes, 10,000; hemoglobin, 50 per cent.

At 11.30 a. m. lumbar puncture was performed, the right knee-joint was aspirated and cultures were made from the blood. From the spinal canal about 20 cc. of turbid, pale-yellow fluid were withdrawn. A specimen was centrifugalized and the sediment, when examined miscroscopically, was found to be made up of leukocytes, with a few red blood-corpuscles. Both within and outside of the leukocytes were seen many diplococci. The cocci were lance-shaped, and occurred in pairs or short chains. They were not decolorized by Gram's method. The fluid aspirated from the right knee-joint was very turbid, yellowish. Microscopic examination showed it to contain numerous leukocytes and many diplococci resembling those found in the spinal fluid. Cultures were made from the spinal fluid on blood-serum, plain agar, and hydrocele agar slants. Cultures from the fluid aspirated from the knee-joint were made in milk and on agar and blood-serum slants. The cultures from the blood were made in the usual way; 8 cc. of blood being obtained and divided among three Erlenmeyer flasks of bouillon.

During the remainder of the day the patient's condition remained about the same. At 8 p. m. the leukocyte count was 15,000.

By the following morning, February 15, the cultures from the blood showed a growth of diplococci which, in shape and staining reactions, were identical with *diplococcus pneumoniæ*. A clinical diagnosis of pneumococcus septicemia, meningitis, and arthritis was therefore made. On this morning the patient was unconscious. The temperature for the previous 24 hours ranged between 104° and 105.2°. The pulse was rapid and weak; the respirations were 36 to the minute. Examination of the lungs showed numerous coarse râles over both lungs, but nowhere tubular breathing. Kernig's sign was present. Leukocytes numbered 6000. Patient's condition gradually grew worse, and death occurred at 2.20 p. m.

In all the cultures made from the blood, spinal fluid, and fluid from

the joint, there was a profuse growth of diplococci. These were subsequently fully tested by growth in various media, and the provisional identification as *diplococcus pneumoniæ* fully confirmed.

Abstract of the pathologic report:

No. 1677, Murray, died February 15, 1901, 2.20 p. m. Autopsy, February 16, 11 a. m.

*Lungs.*—Right: There are a few old adhesions between the lobes. The lower lobe is very œdematous, and contains disseminated minute areas of consolidation. Bronchi are not especially congested. The upper lobe shows a few old scarred tubercles. Left: Also somewhat œdematous. It shows in the lower portions a few minute areas of broncho-pneumonia. This portion of lung floats.

*Abdominal Viscera.*—No abscesses were found, though in places in the pyramids of the kidneys there were a few opaque white lines.

*Brain.*—The dura is adherent to the cranium and is somewhat thickened. On its inner surface it appears brownish, somewhat flecked. The cerebral sulci are filled with a greenish purulent exudate, which also extends over the base, over the lobes of the cerebellum, and to a slighter extent about the medulla and cerebral peduncles. The cerebral ventricles contain only a little, slightly turbid fluid, the third ventricle is rather distended with this fluid, the fourth ventricle shows no abnormalities.

*Spinal Cord.*—No examination could be made.

*Right Knee-joint.*—The capsule contains about 100 cc. of greenish, purulent fluid. The synovial membrane is much injected, and shows a papillary outgrowth of somewhat translucent connective tissue. On exposing the articular surface, the outer condyle of the femur is found to show almost complete erosion of the cartilage, the articular surface consisting of enamel-like bone worn to a mirror surface. The corresponding articular surface of the tibia shows a similar condition. The cartilage over the remainder of the joint on the lateral surface is very much elevated. In some areas this is due to thickening of the cartilage; in others the elevation consists of exostoses covered by a thinner layer of cartilage. There are some slight hemorrhages in the neighborhood of the joint.

Microscopic sections from the articular surface of the bones and tissues about the joints show the characteristic appearance seen in the joints in *arthritis deformans*, and in addition, there is seen a secondary superficial purulent inflammation.

Section from the lungs show small areas of very fresh bronchopneumonia.

In sections from the kidneys are seen several small areas; showing beginning abscess formation.

In cultures made at autopsy from the heart's blood, meninges, kidney, and liver, there was a growth of *diplococcus lanceolatus. Bacillus coli communis* also grew from the kidney. From the consolidated areas in the lung only *B. coli communis* grew. However, in sections made from these areas and stained by Weigert's method, lanceolate diplococci could be demonstrated in considerable numbers.

CASE. III. *Clinical Summary.*—Acute lobar pneumonia (rt. mid-lobe), acute pericarditis (7th day), arthritis of right shoulder (7th day), acute vegetative endocarditis (8th day), meningitis (9th day), arthritis of right ankle (10th day), death (11th day).

W. A. H., æt. 42, male, German, Med. No. 15,749. Admitted June 2, 1903, on the fourth day of the disease, complaining of "fever."

*Family History.*—Negative, except for death of one child from "spasms."

*Personal History.*—Weakly as a child; no definite diseases of childhood beyond some "brain trouble"; pleurisy twice in 1878; typhoid fever in 1901; no other acute infections.

*Head.*—Slight deafness in right ear since childhood; no history of discharge.

*Respiratory.*—Subject to colds; always more or less cough with whitish sputum; no hæmoptysis; frequent night sweats drenching night-gown

*Alimentary.*—Vomited occasionally during past year, irrespective of food; diarrhœa since May 1, 1903, with 4 or 5 watery stools; never contained blood.

*Genito-urinary.*—Micturated once or twice every night for years; œdema of ankle since 1902; denied lues and "tripper"; no history of secondaries.

*Habits.*—Used alcohol to excess since youth, beer, whiskey, etc.; did not use tobacco in any form.

*Present Illness.*—Since the last week of May, 1903, had been feeling out of sorts; general lassitude; anorexia. About May 30 had chilly sensation, but no definite rigor; fever and drenching sweats during the same night. Much cough with fairly profuse muco-purulent sputum, never blood-tinged. Fever had been present since onset, more marked during the day. No nose bleeding. No diarrhœa for past few days.

*Status Presens.*—Admitted at 4 p. m. on June 2, the 4th day of disease. T. 98⅖°, P. 116, R. 24. T. rose to 105.5° at 4 a. m. of 3d inst. P. 116, R. 28.

The note dictated by the resident physician, Dr. McCrae, on June 3, read as follows: "Patient very ill; face flushed; mind dull; pupils equal and active; tongue slightly coated; mucous membranes of fair color; throat somewhat injected with some swelling on left side of uvula.

*Thorax.*—Flat expiration slightly less on right; percussion note over right front and right back slightly impaired; vocal fremitus, if anything increased on right side; breath sounds harsh but clear throughout left lung; rather higher pitched and more prolonged expiration on right

*Heart.*—Point of maximum impulse in 5th interspace 10 cm. from midsternal line. Relative cardiac dulness diminished. Sounds rapid, 1st much like 2d. Pulse 34 to ¼, very small, regular and not dicrotic.

*Abdomen.*—Slightly full; no positive rose spots; spleen not felt.

*Sputum.*—Tenacious, muco-purulent, slightly streaked with fresh blood, microscopically many pus cells, and clumps of bacilli and diplococci, no tubercle bacilli.

*Urine.*—Negative except for slight trace of albumen.

*Blood.*—Negative for parasites; leukocytes, 13,300.

*June 4* (6th day).—T., which fell to 99.6° at noon of 3d, had since ranged from 101.6° to 104.5°. P. 112-132, R. 28-32. Very restless during the night and slightly delirious. Signs of consolidation over right middle lobe more definite. Left lung clear. Heart negative. Leukocytes 10,400. Blood culture at 2 p. m. proved negative.

*June 5* (7th day).—General condition about the same. T. 100.6°-104.2°, P. 96-130, R. 28-40. No change in physical signs of lungs. Heart: A few *suggestive scratches* heard over base of heart synchronous with systole. Pulse difficult to count owing to marked tremor of hands; very soft and small. Complains of pain in *right shoulder joint.* No redness, no swelling; slight tenderness posteriorly. Leukocytes 8100.

*June 6* (8th day).—Temperature rose to 105.5° at 7 p. m. of 5th inst., but fell steadily during the night, reaching normal at 6 a. m. Rather cyanotic. General coarse twitching of both upper extremities. Signs of resolution of consolidated middle lobe. Left lung clear. Heart: Sounds at apex a trifle feeble but clear. Near the sternum in 3d, 4th, and 5th interspaces is heard a *murmur with systole*, which has a curious, somewhat superficial scratching quality, suggesting a pericardial rub but not characteristic; audible at aortic area, where 2d sound is somewhat accentuated. Right shoulder joint painful and tender, but not red nor swollen. Leukocytes 9100.

*June 7* (9th day).—T. 101.5°-104°, P. 108-120, R. 28-48. Patient semicomatose. Pupils equal; no strabismus. Stiffness of neck muscles marked. Arms flexed at elbow. Tendon reflexes of uppers absent. Patellar reflex absent. No ankle-clonus. Babinski's sign doubtful. Kernig's sign marked. Inflammation of right shoulder subsiding. Blood negative for parasites. Leukocytes 10,200.

*June 8* (10th day).—T. 101.4°-103.5°, P. 100-132, R. 28-44. Delirium rather more marked. Pupils equal and active. Does not answer questions. Marked general tremor, retraction, and rigidity of neck. Kernig's sign positive. *Right ankle-joint* shows slight swelling and redness, but no tenderness. Consolidated right middle lobe gradually undergoing resolution. Some areas of purpura over right back. Lumbar puncture, 20 cc. withdrawn under normal pressure, negative in smears and cultures. Blood culture showed heavy growth of pneumococci in plates and flasks in 24 hours. Widal negative.

*June 9* (11th day).—T. 102°-105.7°, R. 28-44, P. 100-140. Patient roused with difficulty. Pulse of fair volume, regular but distinctly *collapsing.* Pupils equal. Twitching of muscles of face, neck, and arms. Other signs of meningitis as before. Right ankle-joint shows more marked signs of inflammation. Heart sounds well heard at apex, second followed by a *diastolic murmur*, of maximum intensity in 2d right interspace, first clear everywhere. Marked pulsation in peripheral vessels; faint capillary pulse. Leukocytes 10,300.

*Aspiration of right ankle-joint* at 7 p. m. yielded 2 cc. of turbid, milky fluid. Typical pneumococci in smears and cultures. Death at 9.05 p. m.

*Autopsy* performed 14 hours after death by Dr. Van Wart.

*Anatomical Diagnosis.*—Lobar pneumonia with gray hepatization (right lung), acute adhesive pericarditis; acute aortic endocarditis with ulceration of aortic valve; acute tricuspid endocarditis; fatty myocarditis; atheroma of aorta and coronaries; cirrhosis of liver; chronic interstital pancreatitis with fat necrosis and abscess formation; chronic nephritis and fatty degeneration of kidneys, acute splenic tumor; meningitis; acute arthritis; hypertrophy of prostate.

*Thorax.*—Left pleura contains 100 cc. of slightly blood-stained fluid. Left lung adherent at apex; right lung adherent at apex and upper part of lower lobe posteriorly. Left lung negative except for healed tubercle at apex. Right lung smaller than normal; scar at apex; middle lobe in condition of gray hepatization.

*Heart.*—Pericardium adherent by recent fibrinous adhesions. Tricuspid valve (13 cm.) showed a large, pale, irregular mass on auricular surface, measuring 1 x 1.5 cm., pedunculated and floating free. Pulmonary and mitral valves normal. The aortic valve (8 cm.) showed slight sclerotic change. The right posterior cusp of the aortic valve showed recent vegetations and considerable ulceration, resulting in the right base of segment being eaten through and floating free. Myocardium soft, pale red, and on tangential section showed yellow streaks. On the coronaries patches of sclerosis.

*Spleen* (130 grammes).—Soft and flabby; mottled; pulp soft and structure made out with difficulty.

*Liver.*—1650 grammes, slightly enlarged and of very irregular shape; on section there is considerable increase in connective tissue arranged about lobules.

*Stomach and intestines* negative.

*Pancreas.*—12 x 2.5 x 1.5 cm.; very firm, cutting with difficulty, except in head near lower border, where there is a small abscess cavity (1.5 x 1 cm.), communicating with duct of Wirsung. Thorughout organ numerous opaque yellow areas with softened center. Connective tissue considerably increased.

*Kidneys.*—Show characteristic changes of chronic nephritis.

*Bladder.*—Negative, urine negative to sugar, hypertrophy of middle lobe of prostate.

Right ankle slightly swollen and on opening it the surrounding tissues were found to be slightly infiltrated with serum. The joint itself contains considerable quantity of purulent fluid, and the cartilage covering it has lost its smooth, glistening appearance. No evidence of extension of the process to the surrounding bone.

*Brain.*—The calvarium more adherent to dura than normal. Dura normal, beyond increase in number of Pacchionian granulations. Cerebrospinal fluid not increased. The pia and arachnoid somewhat opaque, as were the veins in the sulci, but not more so than usually seen in senile or insane brains. Pial arteries prominent. The circle of Willis showed slight sclerosis. Pons, cerebellum and cranial nerves apparently normal.

Sections from various parts of cerebral cortex showed very few leukocytes, otherwise negative. Sections stained by Nissl's method show the usual changes in the Nissl bodies in acute infections.

*Bacteriological Report.*—A. *Clinical.*—The first *blood culture* was taken on the 4th inst., the 6th day of illness; 12 cc. of blood were withdrawn from the median cephalic vein. This was divided between five Erlenmeyer flasks, each containing 150 cc. of medium; three of litmus milk, and two of bouillon. They were incubated for 5 days at 37° C., but proved absolutely sterile.

The second blood culture was taken on the 8th inst., or 10th day of disease; 14 cc. of blood were withdrawn and divided between three flasks of litmus milk, two of bouillon and six tubes of agar-agar. The latter were plated. Next morning all six plates showed very numerous opaque, white, circular, pin-point colonies, which under low magnification showed sharply defined periphery and dark nut-brown color. Smears stained by Welch's method show typical lanceolate dipdococci with fairly definite capsule.

In 48 hours all litmus flasks were acidified and coagulated, and the bouillon was turbid, while the blood was changed to dark olive green color.

The *fluid from the lumbar puncture* taken on the same day was absolutely negative.

*Culture from ankle-joint*, taken two hours before death.—About 2 cc. of blood-stained turbid fluid were withdrawn. This was divided equally between one bouillon tube, one slant agar tube, and one blood serum slant. Smears stained by the ordinary stains showed numerous polymorphonuclear leukocytes, but no diplococci. The tubes were incubated for 12 hours, when 6 agar-agar plates were made. A series of 3 by adding 5 "öses" of bouillon tube to first agar and so on to third dilution. The remaining bouillon was then divided equally between 3 other agar tubes and plated. The slant cultures proved negative, as did the plates in first 24 hours. In 48 hours the first series of plates was negative, but the second series showed a few typical pneumococcus colonies, smears from which were stained and showed typical lanceolate diplococci with well-defined capsules.

The organism isolated from the blood and that from the ankle-joint were run through the various media and showed typical growth in slant agar, glucose agar, potato, bouillon, Dunham's solution, litmus milk, and gelatin. On the former it was chiefly characterized by its very light, almost invisible growth; it acidified and coagulated milk; and in gelatin there was little or no visible growth and absolutely no liquefaction.

A 24-hour agar culture from each was inoculated intraperitoneally into 2 mice. The mouse inoculated with the joint organism died in less than 24 hours, and the organism was recovered in pure culture from the heart's blood, and peritoneum; smears showed beautiful typical capsules and the cultural characteristics were absolutely identical with those of the original stock. The mouse inoculated with the organism from the blood died in about 48 hours, and from its heart's blood and peritoneum diplococci

with their typical cultural characteristic and capsule were demonstrated. This organism was not so virulent owing to the longer interval that had elapsed from its primary isolation.

*B. Post-mortem.*—Owing to the absence of the bacteriologist, Dr. Van Wart asked me to take the cultures.

Pleura, pericardium, and spleen showed pure cultures of *S. pyogenes aureus.*

The *heart's blood* showed few *pneumococci* in smears and on the plates, but transfers showed no growth.

From the vegetations on the aortic cusps, which was previously seared with a red hot knife, a small fragment was broken off and macerated in an agar tube. From it was recovered the pneumococcus with the *B. proteus vulgaris* and *S. aureus.*

The cerebral meninges yielded a pure culture of pneumococcus, and few pneumococci were demonstrated in the smears. The right ankle-joint also contained pneumococci with a few colonies of *Staphylococcus albus.* From the peritoneum: *B. proteus vulgaris, B. coli communis, Str. pyogenes,* and *S. albus.* From the pancreatic abscess: *B. coli communis* and *S. aureus* and *albus.*

In this series, just as in the former, all the ordinary media were employed for identification, the only difference being that the organism was not run through a mouse in every case.

*Historical Note.*—The French Clinicians Fournet (1839), Grissole (1864), and Bouchard (1881) had pointed out the occurrence of an arthritis as a complication of croupous pneumonia before the discovery of the pneumococcus by Sternberg (1881) and Pasteur (1881), or the complete morphological and etiological publications of Fraenkel (1886) and Weichselbaum (1886).

While many authors, as Klebs (1875), Eberth (1881), Osler (1881), Senger (1886), and Fraenkel (1886), had noted the presence of the pneumococcus in meningitis, endocarditis, and nephritis, complicating pneumonia, the first account of it in the joint fluid is given by Foa and Bordoni-Uffreduzzi (3), (1888), who found in "several cases" as a sequel of croupous pneumonia a polyarthritis with a purulent exudate in which a diplococcus was present. Shortly afterwards Weichselbaum (4) in an excellent paper, "Upon Unusual Localization of the Pneumonic Virus," gave the first clinical description of a case with bacteriological findings, autopsy notes, and animal experiments. L. Leroux (5), in his graduating thesis, analyzed the 28 cases in the literature up to the year 1899. Since the latter date each year has seen many additions to the literature. The most important papers are those by Cave (6), Pfisterer (7), and Herzog (14).

## Etiology.

*Incidence.*—Pneumococcic arthritis is a rare condition occurring only 6 times among 4256 cases of pneumonia (0.14%), collected from some European Hospitals (Berlin, Munich, etc.) by Leroux in 1899. Davies and Brown (13) could find but 4 cases of arthritis complicating pneumonia during 10 years at St. Bartholomews Hospital, London; in but 1 of these cases were the data sufficient. During the beginning of the year 1906 Herzog (14) collected from the literature 91 cases, to which one can add 3 more cases (15, 16, 17), making a total of 94 cases up to the year 1906, inclusive. It is worthy of notice how rapidly during the past 5 years the number of cases has increased with the improvement of clinical bacteriological methods; thus while Cave could find but 31 cases up to 1901, 5 years later Herzog collected 91 cases!

*Sex and Age.*—Nearly all authors are agreed that this form of arthritis is commoner in males than females. Cave found 25 males to 3 females; Herrick (8) 40 males to 7 females. The preponderance in the male sex will find a possible explanation later in the rôle that traumatism plays as an etiological factor. It was formerly thought to be an affection of advanced adult life and in 1901 Cave was able to collect but 2 cases under 2 years of age. With the wonderful development in scientific pediatrics during the past 5 years it has been found that pneumococcic arthritis is not such a rarity in infancy and childhood. Dudgeon and Branson (9) in 1903 pointed out that while purulent arthritis is very uncommon in infants during first 6 months of life, yet when present it is almost always due to the pneumococcus. Herzog in 1906 asserts that young children are especially prone to pneumococcic infections of all kinds, and that pneumococcic peritonitis is three times more common in the child than in the adult; further that this liability in infancy is even greater for arthritis; and lastly that the frequency of pneumonia with arthritis in nurslings may account for the fact that an osteomyelites in infancy is more commonly situated in the epiphyses than it is in older children. Herzog collected 28 cases in children under two years, 8 under fourteen years, and 55 cases in adults. A striking contrast to the figures of Cave! Hence we can no longer consider pneumococcic arthritis more common in adult life than in infancy, though we are not yet warranted in assuming the contrary.

*Predisposing Factors.*—The close parallel between the peritoneum and synovial membrane of the joints in structure and liability to disease in acute infections has long been recognized. Apart from this susceptibility of the synovial membrane of the joint, it is possible that in certain cases the establishment of a *partial immunity* to the pneumococcus results in the production of local lesions rather than a continued septicæmia. This theory is supported by Bezançon and Griffon, who succeeded in producing experimentally an arthritis in rabbits by a preliminary partial immunization with small doses of a pneumococcus culture of diminished virulence, followed subsequently by a full dose of a virulent culture. *Traumatism and Previous Disease of the Joint,* unquestionably play a rôle, at least in the site of election, in the etiology of arthritis in pneumonia. Leroux found a history of a "point d'appel" in 10 out of 28 cases (35%); Cave in 10 out of 31 cases (32.2%); Cole in 13 out of 41 cases (31.7%); Pfisterer in 35 cases found a history of trauma 3 times and gout or rheumatism 6 times (25.7%). Herrick in 21 cases found trauma in 5 cases and either plumbism alone or plumbism with gout in 2 cases (33.3%). The rôle of trauma according to Herzog is more important in adults as shown by the greater frequency with which males are affected; but Larrier (14) has reported a case of pneumococcic arthritis in an infant with a previous history of trauma. In addition to this clinical evidence, it has been shown by animal experimentation that it is difficult to produce an arthritis without first causing a "locus minoris resistentiæ" by injury to the joint proper or by section of the nerve supplying the extremity in question.

*Pneumonia.*—Pneumococcic arthritis can be classified according as to whether the arthritis occurs as a complication or sequela of a pneumonia, as a precursor of the pneumonia or lastly as independent of an inflammation of the lungs.

I. The *meta-pneumonic* cases, or those in which the arthritis is a complication or sequela of an acute lobar or lobular pneumonia, comprises the vast majority of cases. Thus Cave found that 28 out of 31 (90.3%); Pfisterer 26 out of 30 (86.6%); and Herzog 71 out of 91 cases (78%) belong to this group.

II. The *præ-pneumonic* cases or those in which the arthritis precedes the pneumonia are very rare, and to me somewhat questionable. Herzog could find only four in literature and was able to add one of his own (5.5%).

III. The *non-pneumonic* cases or those in which the arthritis occurs quite independently of an inflammation of the lung tissue proper, are uncommon as compared with the first group, but much more common than the præ-pneumonic cases. Thus Herzog collected 15 cases (16.4%) from the literature.

It is noteworthy that both groups II and III are more common, relatively and absolutely, in infancy and childhood than in adult life, where they are a rarity. Thus Herzog found in 28 cases of infants under 2 years, 11 cases with no *previous* pneumonia (39.3%), in 8 children between 2 and 14 years 5 cases with no previous pneumonia (62.5%), while in 55 adults there were only 4 cases without a previous pneumonia (7.3%).

## Pathogenesis.

The *portal of entry* in the first group—the meta-pneumonic—is undoubtedly the respiratory tract. In those cases occurring independently (groups II and III) of pneumonia, the pneumococcus may gain an entry by the bronchial mucous membrane, the mouth, the tonsils, nose and its sinuses, the middle ear, the conjunctiva or even the peritoneum, especially when any one of these be inflamed as occurs in bronchitis, stomatitis, angina catarrhalis, otitis media, etc. In children Herzog (14) believes the commonest portal of entry is the middle ear and quotes Kössel, of Berlin, who in 108 autopsies in children under 1 year found the middle ear diseased 85 times (78.7%), while Ponfik found the same condition in 91%. Further, Hartmann found 85% of living nurslings with otitis media. Zaufal and others have found 40% of the cases of otitis media in children to be due to the pneumococcus.

*The path of infection* from the primary focus to the "locus minoris resistentiæ" is either the blood or possibly the lymph stream. In the majority of cases, especially in the first group, the *blood stream* must be the path by which the pneumococcus is carried from the diseased lung to the joints in an analogous way to the mode of infection in acute osteomyelitis. The fact that the great majority, if not all cases of pneumonia, are accompanied by a true septicæmia has long been recognized. Granting this, it is not difficult to imagine how a previously diseased joint, or one rendered susceptible by injury, however slight (as the mere strain of lifting or turning the patient in bed), may become suitable for the local production of the invading organism.

The rôle played by the *lymph-stream* is suggested by Pfisterer (7), who pointed out that in 7 cases of *unilateral* pneumonia, the shoulder joint in all and the sternoclavicular in 3 cases were affected on the same side. While we must admit the possibility of the latter, we believe that the blood stream is the usual path of infection.

### Morbid Anatomy.

The arthritis may be monarticular or polyarticular. A monarthritis was found by Cave 19 times (61%), and by Cole 28 times (68%); while a polyarthritis was found by these authors 12 and 13 times respectively. The joints of the upper extremities alone are twice as commonly affected as those of the lower extremities alone, as pointed out by Leroux (11 to 5 or 2.2 to 1), Cave (14 to 10 or 1.4 to 1), Pfisterer (22 to 8 or 2.75 to 1), and Herrick (23 to 18 or 1.75 to 1). An involvement of one or more joints in both the upper and lower extremities is not rare and occurred according to Cave in 7 cases (22.5%), and Herrick in 11 cases (21.1%). Of the individual joints, the larger ones seem more susceptible than the smaller, and of all joints the shoulder and knee are most often involved; thus Pfisterer found involvement of the shoulder 9 times (41%), and of the knee 4 times (18%), in 22 cases; Herrick, involvement of the knee 22 times (42%) in 52 cases; and in 28 infants Herzog found the knee diseased 10 times (36%), the shoulder 7 times (25%), the elbow 4 times (14%), and the ankle twice (7%). Of the smaller joints the sternoclavicular joint was involved 8 times in 52 cases (15%), according to Herrick.

*Character of the Fluid.*—The fluid varies from serofibrin to pure pus according to the stage of the disease or the severity of the case. In some cases the fluid is clear and enclosed in a gelatinous membrane of fibrin and pus cells. In other cases the fluid is fairly thick, yellow to slightly greenish in color, odorless and with a great tendency to fibrin formation as is seen in empyæmata. In some cases the pus is thin, turbid and even deeply blood-stained. We cannot agree with Dudgeon and Branson (9) who lay a good deal of stress upon the prognostic value of the character of the fluid.

*The Interior of the Joint.*—The synovial membrane is usually very swollen and reddened in the advanced stages at least. The periarticular region is also very often affected, while the cartilage and bone are only exceptionally attacked and that in chronic cases.

Symptomatology.

*Time of Occurrence.*—In the meta-pneumonic cases the arthritis may occur on any day of the 1st to the 9th week; thus Pfisterer found 14 cases in which the arthritis had occurred during the 1st 9 days of the pneumonia; in 7 cases the arthritis had developed during the 10th to the 16th day, and in one case the arthritis was not noticed until the 9th week after the onset of pneumonia. In the 2d and 3d group of cases the arthritis ushers in the disease.

*Onset.*—Musser (10) says the onset of an arthritis *in the course* of a pneumonia is indicated by an increased rise in temperature or a chill. This is not always the case and the temperature curve may remain unaltered, the first indication of an involvement of a joint being the complaint of the patient or the local signs. If the arthritis develops after the crisis has occurred, there is a chill sometimes, and a return of fever almost always. In many cases an endocarditis or a pericarditis develop at the same time.

*General Symptoms.*—The picture is usually one of a severe toxæmia with delirium or dulness of the sensorium, moderate or irregular fever, moist skin or even actual sweats, rapid and often thready pulse —in short what one always finds in a severe infection—of which the arthritis is after all only an expression. In children, according to Branson, the constitutional symptoms only in the severest cases keep pace with the extent of the local lesion; thus an infant may eat and sleep well—a condition of affairs quite inconceivable in staphylococcic or streptococcic arthritis. Further in children, even when there is high fever, there may be an intense pallor, resembling that in empyæma.

*Locally.*—Pain is not as a rule a prominent feature, though in many patients owing to the dulling of the sensorium the degree of pain is difficult to determine. The two chief characteristic signs are marked swelling of the periarticular region and slight redness of the overlying skin. This periarticular œdema is pronounced in the subacute cases. In same cases the inflammation is confined to the periarticular structures, as the subdeltoid bursa (Herrick). The general appearance of the joint resembles in many instances that of gonorrheal arthritis. In infants, according to Branson, there is nearly complete absence of the periarticular inflammation and brawny œdema; while on the other hand, Herzog emphasizes the presence of marked swelling and inflammatory œdema in the neighborhood of the

joint or even the entire affected extremity, in addition to heat and tension *without* circumscribed redness.

*Diagnosis.*—A provisional diagnosis in the majority of cases is very simple. A patient, during the course or convalescence of pneumonia, with pain, swelling in the periarticular region and slight redness of the overlying skin, may be strongly suspected of suffering from a pneumococcic arthritis. But an absolute diagnosis cannot be made without aspiration of the affected joint and a complete bacteriological examination of the fluid, viz., film preparations, cultural characteristics, and animal inoculation. As a rule the typical lanceolate diplococci are readily found and rarely present the difficulty that occurs in the discovery of the gonococcus. The capsules, however, cannot be readily seen, but the positive reaction to Gram's differentiates them from Neisser's coccus. For the primary cultivation ordinary blood-serum, blood-agar, or glucose-bouillon are the best media. Beef blood-serum, upon which the pneumococcus appears as yellow to light brown colonies in contrast to the colorless growth of the streptococcus, is warmly recommended by von Brunn.

When the organisms are very scarce, we have found a very good method is to add about 5 cubic centimeters of the joint fluid to about 10 cubic centimeters of bouillon; place in the thermostat 8 to 10 hours and then from this make plain agar plates as was done in Case III of our series. Having once obtained a growth, which is usually in pure culture, the cultural characters should be studied on the various media.

Lastly a mouse should be inoculated subcutaneously and the heart's blood examined microscopically, when the typical capsules will be seen distinctly. Naturally also the cultural characteristics of the organism from the heart's blood should be found to correspond to those of the primary cultivation.

*Differential Diagnosis* is not always easy. *Staphylococcic* and *streptococcic arthritis* present the first difficulty; here the symptoms, especially the constitutional, are more severe, as evidenced by the high fever, vomiting, septic facies, etc. An examination of the fluid is however absolutely necessary.

*Gonorrheal Arthritis,* especially in the nursling resembles pneumococcic arthritis, for they both may be polyarticular, but in the former there is usually a primary conjunctivitis or vulvitis, the periarticular œdema is slight and the pus is thin and serous.

*Acute Rheumatic Arthritis* is very rare in nurslings (5 cases in 1500 infants, according to Herzog) and the joint symptoms are usually slight, while endocarditis is common. In adults the multiplicity of the joints involved, the fugacious character of the involvement, the exquisite pain and the presence of the other rheumatic stigmata, tonsilitis, endocarditis, pericarditis, or the various erythemata, and lastly the character of the joint fluid will settle the diagnosis.

*Luetic Arthritis* in a nursling may give some difficulty, but here the symmetrical and painless involvement of the joints together with the common luetic stigmata should be sufficient evidence.

*Tuberculous Arthritis,* especially when accompanied by pulmonary signs and fever, is very misleading. The history of the case, but above all the examination of the joint fluid for tubercle bacilli will clinch the diagnosis.

*Prognosis* is usually grave, depending rather upon the extent and the virulence of the pneumococcic infection, of which the arthritis is an expression, than upon the arthritis *per se.* However, the prognosis is better when only one joint be affected and when there is no other metastatic focus than when several joints are involved or a pericarditis or endocarditis coexist. Thus Cole found that among 16 patients with a monarthritis and no other focus of infection 10 recovered, while of 18 with multiple foci only 1 recovered. The prognosis is better in children than in adults according to von Brunn. On the other hand Davies and Brown (13) point out that the mortality from pneumonia itself is greatest in early life and quote Kanthack and Lance who found that 64% of 170 fatal cases of pneumonia were under 21 years of age. However, in adults, the mortality of pneumococcic arthritis is variously estimated from 55-65%, while that in infancy according to Herzog is but 39%; hence we must agree with von Brunn that the prognosis is a good deal better in early life.

If recovery occurs the course is long and slow and ankylosis of the joint usually results.

*Treatment.*—In addition to the general indication to combat the pneumonia and to support the system (*i. e.,* general hygienic and stimulating measures), we have one of two alternatives to meet the joint condition.

*Palliative measures* in the shape of immobilization and pressure are warmly recommended by Netter and Herrick. Cold locally, in the form of an ice-bag, should also be tried.

*Radical Treatment.*—In the majority of the cases the condition of the patient does not warrant an operation, and the arthritis is but of minor importance. Yet in certain cases, especially in children, where the process is confined to one or two joints and where there are no other metastatic foci, operation under local anæsthesia is certainly indicated. The operation should be restricted to mere opening and cleansing of the joint cavity, with as little disturbance to the joint as possible.

LITERATURE.

1. COLE. Am. Med., 1902, III, 905-908.
2. HOWARD. Johns Hopkins Hosp. Bull., 1903, XIV, 303-306.
3. FOA and BORDONI-UFFREDUZZI. Ztschr. f. Hyg., Leipz., 1888, IV, 67-93.
4. WEICHSELBAUM. Wien. med. Wchnschr., 1888, XXXVIII, 1177; 1209.
5. LEROUX. Thèse de Paris, 1900, 137.
6. CAVE. Lancet, Lond., 1901, I, 82-86.
7. PFISTERER. Jahrb. f. Kinderh., 1902, LV.
8. HERRICK. Am. J. M. Sc., Phila., 1902, CXXIV, 12-34.
9. DUDGEON. Lancet, Lond., 1903, II, 266.
10. MUSSER. Nothnagel's Practice, Am. Ed., 1902, IV.
11. MEYER. Mitt. a. d. Grenzgeb. d. Med. u. Chir., Jena, 1903, XI, 140-158.
12. VON BRUNN. Berl. klin. Wchnschr., 1904, XLI, 721-724.
13. DAVIES and BROWN. Lancet, Lond., 1904, II, 1017-1020.
14. HERZOG. Jahrb. f. Kinderh., 1906, LXIII, 446-469.
15. SECRETAN and WRANGHAM. Brit. M. J., Lond., 1906, I, 915-917.
16. RAW. Brit. M. J., Lond., 1906, I, 1400.
17. MIDDLETON. Brit. M. J., Lond., 1906, II, 197.

# PNEUMOCOCCUS MENINGITIS.

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Meningitis caused by the *Diplococcus pneumoniæ* is usually described as a complication of lobar pneumonia. This is a convenient, though not a strictly accurate, classification, for in a very considerable number of cases pneumococcus meningitis occurs quite independently of lobar pneumonia. In the present series of 25 cases, comprising the experience of the Johns Hopkins Hospital for the past 20 years, 7 cases of meningitis due to the *Diplococcus pneumoniæ* have occurred in which clinically and at autopsy there was no evidence of lobar pneumonia. Thus it is found that 28 per cent of the total number of pneumococcus meningitis cases were uncomplicated by lobar pneumonia. It is necessary, therefore, in estimating the frequency of meningitis as a complication of lobar pneumonia, to exclude those cases of meningitis in which lobar pneumonia is not definitely proved. It must also be borne in mind that lobar pneumonia may be the terminal phase of pneumococcus meningitis.

Excluding then the 7 cases of meningitis, which neither clinically nor pathologically showed evidence of lobar pneumonia, it is found that in a total admission to the medical wards of 728 cases of lobar pneumonia from May 15, 1889, to May 15, 1909, 18, or 2.4 per cent, were complicated by pneumococcus meningitis. "Musser and Norris (Osler's system), in an analysis of 49,028 clinical cases of lobar pneumonia, found pneumococcus meningitis as a complication in .24 per cent, while among 4883 autopsies 3.5 per cent showed meningitis."

In the present series of 25 cases the *Diplococcus pneumoniæ* was demonstrated in the cerebro-spinal fluid by lumber puncture in 16 instances. In 2 cases the fluid failed to give evidence of a meningitis subsequently found at autopsy; in both instances only one lumbar puncture was performed. Lumbar puncture was not performed in 7 cases, but in 6 of these the *Diplococcus pneumoniæ* was found postmortem in the meningeal exudate. Two cases have been included in

this series in which the *Diplococcus pneumoniæ* was apparently not demonstrated. Both cases were clinically and at autopsy lobar pneumonia with meningitis. Weighing all the evidence carefully, it has seemed imperative from the statistical standpoint to include these 2 cases. This has been done reluctantly, however, for in the diagnosis of pneumococcus meningitis the demonstration of the *Diplococcus pneumoniæ* in the cerebro-spinal fluid is the *sine qua non.*

Autopsies were performed on 20 of the 25 cases of this series.

In the experience of the Johns Hopkins Hospital no case of proved pneumococcus meningitis has ever recovered. The disease has been of low incidence, but of absolute mortality.

*Sex.*—18 (72 per cent) were males; 7 (28 per cent) females; a disproportion to be attributed partially to the greater number of male admissions to the medical wards.

*Age.*—No age is exempt, nor does any age show a striking susceptibility. The youngest case was three months old; the oldest 73 years. The first seven decades were represented as follows: First 20.9 per cent, second 12.5 per cent, third 16.6 per cent, fourth 16.6 per cent, fifth 16.6 per cent, sixth 12.5 per cent, seventh .4 per cent.

*The symptomatology* of pneumococcus meningitis presents no characteristic deviation from the well-known picture of meningitis due to other affections: headache, vomiting, slow pulse, cervical and general muscular spasticity, tremors, delirium, convulsions—these are symptoms which may present themselves in the course of meningeal inflammation of whatsoever causation. The *onset* of pneumococcus meningitis is frequently very insidious. It was so in 6 cases of this series, and in 2 cases the symptoms produced were so meager and equivocal that the autopsy alone gave the first indication of meningeal infection. This is scarcely a cause for wonder, for meningitis complicating a disease like lobar pneumonia, where the toxic features so frequently predominate, may easily be masked by the existing toxemia. Lumbar puncture should be resorted to with very slight symptomatic provocation.

*Source of the Meningeal Infection.*—Blood cultures have taught us that pneumonia is a septicæmia. In all probability it is, in the great majority of cases, a septicæmia secondary to pneumonic inflammation. Other structures, however, may be the seat of pneumococcic infection without the lungs being involved. Thus arthritis, conjunctivitis, infection of the maxillary, sphenoid, and ethmoid sinuses, synovitis, and finally meningitis are not infrequently caused by the *Diplococcus pneu-*

*moniæ* independently of pneumonia. Seven cases (28 per cent) of this series showed meningeal involvement without pneumonia. In 3 of these 7 cases no primary focus of pneumococcic infection could be found (Nos. 7778, 18961, 22204); in one case (No. 16592) the patient has a chronic, discharging sinus over the left buttock, but no causative connection was ever demonstrated between this sinus and the terminal meningitis. Caries of the teeth, infection of the right sinus maxillaris and sinus sphenoidalis with extension to the meninges was apparently the successsion of events in another case (No. 17759). In a child of six the terminal meningitis was secondary to a suppurative process in the nasal mucous membrane, ethmoid and sphenoid sinuses. The *Diplococcus pneumoniæ* was demonstrated in the purulent discharge.

The cases in this series were carefully analyzed with the purpose of determining, if possible, *which period of pneumonia is most liable to be complicated by meningeal involvement.* It was found impossible to formulate any reliable rule; the initial symptoms may be meningeal, preceding the signs of pneumonia (No. 22204), or meningitis may develop in a patient apparently perfectly convalescent (No. 16805). In general it may be said that the majority of cases develop during the fastigium of the pneumonia, and the earlier developed the more outspoken the symptoms. Pneumococcus meningitis is, as a rule, a rapidly fatal malady. The patient rarely lives a week; more often death ensues in from one to three days.

For the purpose of *diagnosis* lumbar puncture should be freely employed, for it affords the only means of reaching an exact diagnosis. With ordinary asepsis it is a perfectly harmless proceeding. Quincke states that he has never seen a serious untoward effect.

*Associated Complications.*—Lobar pneumonia was present in 18 (72 per cent) of the 25 cases. In 6 cases (33.3 per cent) the involvement was of an upper lobe, either alone or with other lobes. Pneumonia, of all the acute infections, causes the highest percentage of ulcerative endocarditis. Seven (38.8 per cent) of the 18 cases of lobar pneumonia in this series were complicated by acute ulcerative endocarditis. In the 7 cases of meningitis uncomplicated by pneumonia not a single instance of endocarditis occurred. The aortic valves were affected in all 7 cases, while the mitral and tricuspid valves were each but once involved. The endocarditic cases, with one exception, occurred in males above 35 years of age, which may account for the more fre-

quent involvement of aortic valves. Arthritis complicated 2 cases; in one of these the arthritic lesion was apparently primary and formed the nidus of infection to which the meningitis was secondary. Purulent panophthalmitis was present in one case. It is remarkable that empyema did not occur in a single case of this series.

*Cerebro-spinal Involvement.* The meninges of the convexity, base, and cord may all be involved, thus accounting for the great variety of symptoms. The brain was examined post-mortem in 19 cases; in 18 the meninges of the convexity contained a purulent exudate. The base showed involvement in 17 of the 19 cases examined. The cord was investigated in 13 cases; in 10 there was definite meningitis, while in three the meninges were apparently unaffected.

Case 1.—Lobar pneumonia (rt. lower); very insidious onset of meningitis; delirium and urinary incontinence the only indications of meningeal infection.

Med. No. 2679. Male, æt. 26. Occupation, coal passer on steamship.

Admitted January 21, 1893, complaining of pain in chest, cough, and dyspnœa.

*Family and past history* were negative.

*The present illness* began 10 days before admission with a chill.

*Physical Examination.*—On admission the temperature was 105° F., and patient appeared quite ill. Examination of chest revealed signs of general bronchitis and pneumonic consolidation in the right lower lobe. Leucocytes were 60,600. The sputum contained many encapsulated diplococci. On the day following the temperature fell to 101.6° F., but rose again in a few hours to 105.3° F. The temperature continued high, but the patient seemed somewhat improved until the night of January 24, when slight delirium developed. This disappeared on the following day, but on January 26 slight incontinence of urine appeared. There were now signs of pneumonic involvement of the right upper lobe. The patient's condition grew worse during the day of January 27; the pulse was more rapid and feeble, and the respirations were 60 to the minute. The face was cold and clammy. The temperature had been gradually falling for several days, reaching 99.4° F. at 6 a. m. on the 27th. It rose to 102° F. at 6 p. m., falling again to 99.8° F. at 10 p. m. The pulse rate, which had varied between 116 and 136, increased to 156 on this day. Death occurred at 11.40 p. m., January 27, seven days after admission.

The only symptoms pointing to involvement of the central nervous system were delirium, which was neither constant nor violent, and the incontinence of urine.

*Autopsy No. 384.*—Anatomical diagnosis: "Acute fibrinous and serous pleurisy with exudation; chronic pleurisy; compression of lung; chronic interstitial pneumonia; chronic perihepatitis; swelling of the intestinal lymph tissue; acute meningitis."

*Bacteriological Report.*—Smears made from the pleural exudate showed numerous diplococci and short chains of cocci. Smears from the meningeal exudate showed a few doubtful diplococci.

*Cultures* made from the pleural and meningeal exudates showed pure growths of the *Diplococcus pneumoniæ.*

Case 2.—Lobar pneumonia (rt. upper); meningitis with violent delirium.

Med. No. 3549. Male, æt. 73. Occupation, stevedore.

Admitted December 16, 1893, complaining of cough and pain in the chest.

*Family and past history* were negative.

*The present illness* began six days before with a shaking chill and headache. This was soon followed by pain in the chest and severe cough.

*Physical Examination.*—On admission the temperature was 100.8° F., pulse 129, respirations 40. The patient was delirious. Pectoral examination revealed signs of consolidation at the right apex. On the following afternoon the patient's condition grew rapidly worse, violent delirium developed, and he was with great difficulty restrained in bed. These symptoms continued without abatement during the day of December 18, and the patient, gradually sinking, died at 6 p. m. The temperature rose during the day from 102.5° F. to 104.2° F.; the pulse from 116 to 162; the respirations increased to 68. The delirium was the only symptom indicating the involvement of the central nervous system.

*Autopsy No. 478.*—Anatomical diagnosis: "Acute lobar pneumonia (gray hepatization); acute pleurisy; acute fibrino-purulent meningitis; arteriosclerosis; hypertrophy of the heart; dilatation of both auricles; œdema of the lungs, muco-purulent bronchitis; sclerosis of the pulmonary artery; acute splenic tumor; parenchymatous degeneration of kidneys and liver; hypertrophy of the prostate; dilatation of the bladder, ureter, and pelvis.

*Brain.*—The dura was firmly adherent to the skull cap, especially along the longitudinal sinus. The lateral and longitudinal sinuses contained dark clots. On the convexity of the brain there was a gray exudate, especially marked between the convolutions. The vessels of the pia were injected. The exudate could be stripped off with the meninges, leaving the brain quite pale. A similar exudate was present over the inferior lobe of the cerebellum. The ventricles were not dilated. The spinal cord was not covered by exudate.

*Bacteriological Report.*—The *Diplococcus pneumoniæ* was demonstrated in the lung and in the meningeal exudate.

Case 3.—Lobar pneumonia (rt. upper); meningitis; acute ulcerative endocarditis of aortic valves.

Med. No. 4663. Male, æt. 41. Occupation, laborer.

Admitted January 25, 1895, complaining of cough, hiccough, pain in chest, and loss of weight.

*Family history* unimportant.

*Past History.*—Denied all venereal contagion. Admitted the use of alcohol since his 20th year, often indulging to excess. There was no history of previous acute illnesses.

*The present illness* began six weeks ago with hiccough and cough. At that time the patient was doing light work and he continued to work for one week after the onset of these symptoms. Since then he has been unable to work, owing to gradually increasing weakness. The hiccough has been a constant and distressing symptom. He has had a severe cough, worse in the morning, and has been very short of breath. For the past three weeks he has suffered with severe pain in the upper part of the right chest on coughing, and every evening for the past week he has had a rather severe chill.

*Physical Examination.*—On admission the patient was found to have signs of consolidation of the right upper lobe and a faint murmur was audible over the aortic interspace. The temperature was 98.2° F. at 2 p. m., the day of admission, but rose rapidly, reaching 104° F. at 10 p. m. It fell to 100.4° F. at 10 a. m. on January 26, but rose during the afternoon, reaching 105.8° F. at 8 p. m. At 6 p. m. on January 26 patient was found unconscious in a low muttering delirium, with respirations somewhat labored and Cheyne-Stokes in type. There seemed to be no paralysis of the face or limbs. The right arm was flexed at the elbow and could be extended only with great difficulty. The other limbs were flaccid. The diastolic murmur noted over the aortic area on admission was now very loud and rough. The patient's condition gradually grew worse, the pulse becoming weaker and intermittent. The right arm remained contracted and at times one or the other of the extremities showed marked spastic rigidity. Unconsciousness persisted until death. The temperature continued high, being 105.6° F. at 4 a. m., when death occurred.

*Autopsy No. 619.*—Anatomical diagnosis: "Croupous pneumonia of right lung with multiple abscesses; acute ulcerative endocarditis affecting the aortic valves, with rupture of one of the segments; chronic fibrinous pericarditis; chronic fibrinous orchitis; purulent meningitis.

*Brain.*—Examination of the brain revealed a purulent exudate between the meninges of the convex surfaces. There was slight increase of fluid at the base of the brain. The ventricles were normal.

*Bacteriological Report.*—Smears made from the consolidated portion of the lung, from the abscess of the lung, from the vegetations of the aortic valves and from the pus in the meninges all showed the presence of encapsulated diplococci, having the characteristic shape and staining reaction of the *Diplococcus pneumoniæ*. In the meninges the organisms were often present in large numbers within the leucocytes.

*Cultures* made from the abscesses in the lung showed large numbers of diplococci, presenting the characteristic shape of the *Diplococcus pneumoniæ*. Cultures from the aortic vegetations, meningeal exudate, spleen, and liver remained sterile.

Case 4.—Pneumococcus meningitis, apparently primary; no lobar pneumonia.

Med. No. 7778. Male, æt. 44. Occupation, carpenter.

Admitted September 1, 1897. The patient was delirious on admission, and the history was obtained from his brother.

*Family history* unimportant.

*Past History.*—The patient had always been a strong, healthy man, with the exception of an attack of typhoid fever, complicated by pneumonia, at the age of 22. During this illness he was very delirious.

*Present Illness.*—For three or four weeks before present illness the patient had a cold and was very hoarse. He had not coughed much and was able to prosecute his work as a ship carpenter, working in the hold of a vessel, where it was quite cold. He seemed well on Saturday, August 28. The onset of the present illness was marked by a chill, which developed suddenly in the afternoon of August 29, three days before admission. The patient did not complain of pain, but on the following day he felt too weak to go to work. Delirium developed in the afternoon of this day and continued until admission.

*Physical Examination.*—The patient was quite delirious, would not answer questions, groaned occasionally as if in pain, and at times became very noisy. He lay with his head turned to the right side and resisted any effort to turn it. The face and head were covered with a profuse perspiration. The cheeks were flushed. There was no strabismus or nystagmus; the pupils were widely dilated, apparently inactive. The patient occasionally gave a short cough, raising a small amount of sputum, which was not bloody. The arms were flexed at the elbows and attempts to extend them were stoutly resisted. Examination of the chest revealed an area of dulness in the righ axilla and lower back. Over this area the breath sounds were harsh, but nowhere tubular. The heart sounds were clear. The pulse was weak and only 36 to the minute. The abdominal muscles were held very stiffly; the spleen was not palpable. The leucocytes numbered 13,800; temperature 104.8° F.; respirations 64. At 11 p. m. there seemed to be more retraction of the head, and the patient held himself very rigidly, lying by preference on the right side and resisting any attempt to turn him. Deglutition seemed difficult. During the next few hours the patient's condition grew rapidly worse; the head was markedly retracted; the arms were held stiffly; the body, however, was relaxed. The reflexes were not increased. Gradually becoming weaker, the patient died at 12.40 a. m. The temperature at the time of death was 105° F.

*Autopsy No. 989.*—Anatomical diagnosis: "Acute fibrino-purulent cerebro-spinal meningitis (*Diplococcus pneumoniæ*); chronic pachymeningitis; acute splenic tumor; chronic diffuse nephritis, general *Diplococcus pneumoniæ* infection; fatty degeneration of the liver."

*Brain.*—"The dura is not adherent to the calvarium. The subdural space, especially about the base, contains about 100 cc. of turbid, flocculent, yellow fluid. The surface of the pia over the vertex is smooth for the most

part. It is stripped from the brain with some difficulty. In the sulci under the pia, especially well marked in Broca's region and about the basal ganglia, there is an accumulation of opaque, yellow, fibrino-purulent material. The third ventricle contains a small amount of yellow, purulent fluid. The ventricles are not distended." The cord was not removed, but the fibrino-purulent exudate could be seen extending well into the spinal meninges.

*Bacteriological Report.*—"Smears made from the meningeal exudate showed many pus cells, about which were numerous diplococci, distinctly lanceolate in shape, some showing capsules."

"*Cultures* made from the liver, kidney, spleen, heart's blood, ventricles of the brain, and the meningeal exudate all showed many granulating colonies which were composed of diplococci of distinctly lanceolate shape, many of them having capsules."

Case 5.—Primary pneumococcus meningitis.

Med. No. 8464. Female, æt. 6.

Admitted March 31, 1902, complaining of pain in head, back, legs, and arms.

*Family History.*—The mother died four days before the patient's admission to the hospital with what seems to have been pulmonary tuberculosis. There was no further family history of tuberculosis.

The *past history* was unimportant.

*Present Illness.*—Five days before admission to the hospital, after eating supper, the patient vomited, appeared feverish, and at 10 p. m. became delirious. She remained delirious up to time of admission. She had apparently severe frontal headache and pain in the back of neck. The neck had been stiff, and for three days prior to admission there was distinct retraction.

*Physical Examination.*—The head was distinctly retracted; the pupils were of medium size and equal. There was definite bilateral internal strabismus. The heart and lungs were found to be normal. The patient's condition remained about the same until April 17. The temperature continued elevated, somewhat irregular, rising at times as high as 104.5° F., and never falling to normal. On April 17 a definite rash was noted over the face, neck, thorax, arms, and upper thighs. The rash was erythematous in character and in places papular. This rash disappeared after two days. A purulent conjunctivitis and a profuse purulent discharge from both nostrils now developed. Smears from the discharge showed cocci, occurring often in lanceolate pairs, and in groups. Cultures, however, gave a pure growth of *Staphylococcus pyogenes aureus*. On April 18 the temperature dropped from 104° F. to 98° F. and continued subnormal during the remainder of the course. On April 20 the child's mental condition seemed somewhat better; she could be roused. The retraction of the head, on the contrary, was even more marked than it had previously been. The pulse grew gradually more rapid and weaker, and death occurred at 8 a. m., April 21. At no time were there any signs of pulmonary involve-

ment, and the heart sounds remained clear. Lumbar puncture was attempted on two occasions, but no fluid was obtained at either time.

*Autopsy No. 1082.*—Anatomical diagnosis: "Cerebro-spinal meningitis; suppuration of nasal mucous membranes, ethmoidal, and sphenoidal sinuses; internal hydrocephalus; lobular pneumonia."

*Brain.*—"On reflecting the dura the meninges over the convexity are turbid. The turbid fluid is accumulated especially in the sulci. The base of the brain is covered with a thick, yellowish-white, soft, pus-like exudate. The exudate extends from within 2 cm. of the optic commissure over the pons, medulla, and edges of lateral lobes of cerebellum. The spinal cord is covered with exudate, which is thickest over the posterior surface, where the exudate is yellow and creamy. The fourth and lateral ventricles contain an excess of turbid fluid. There is pus in the ethymoid and sphenoidal sinuses, and the mucous membrane of nose is hyperæmic and covered with thick pus."

The *Diplococcus pneumoniæ* was found in the pus from the nasal mucous membrane and sinuses, from the cerebro-spinal exudate, and in the lungs.

*Bacteriological Report.*—Cover slip preparations from the exudate over the base of the brain showed a few diplococci, not typically lanceolate, lying both intra- and extra-cellular. They stained by Gram.

*Cultures* made from this exudate on agar remained sterile. Cultures from the lungs, nasal mucous membranes, and pus from the sphenoidal sinuses yielded a growth of *Diplococcus pneumoniæ*.

The accuracy of the bacteriological findings in this case is certainly open to question. There are several clinical features which strongly suggest that the case was one of infection with the meningococcus. The case illustrates the difficulty which may occasionally arise in the etiological differentiation of meningitis, and should accentuate the wisdom of giving every meningitis patient the benefit of the doubt by using, if possible, the Flexner anti-meningococcic serum.

Case 6.—Meningitis with the *Diplococcus pneumoniæ* and *Diplococcus meningitidis* in the cerebro-spinal fluid; very insidious onset.

Med. No. 9652. Male, æt. 33. Soldier.

Admitted March 11, 1899. The patient was unconscious on admission, and the following history was obtained from his friends:

*Family and past history* were unimportant.

*Present Illness.*—The patient had been a soldier in the regular army, stationed in Georgia, and had returned to Baltimore 11 days before admission. He had complained of occipital headache ever since his return, but this caused him only slight discomfort until four days before admission, when it became so severe that he was compelled to go to bed. He had also had a slight cough and pain in the chest which was not at all severe. Expectoration was small in amount and was not bloody. He had vomited twice since the onset. The evening before admission he fell into a restless delirium.

*Physical Examination.*—The patient was semi-conscious, tossing about in bed and moving his arms and legs constantly. He did not respond to questions. The temperature was 102.6° F.; pulse 84; respirations 36; leucocytes 19,300. The pupils were of moderate size, equal, and reacted feebly to light and accommodation; no strabismus. There was marked stiffness of the neck and some rigidity of the extremities. Examination of the lungs and heart was entirely negative. The reflexes were normal. On the morning of admission lumbar puncture was first performed and 20 cc. of purulent fluid removed. Cover slip preparations made from sediment showed intra-cellular diplococci. On the following day the patient seemed brighter, apparently understood questions, but could not respond. The restlessness had greatly decreased. Upon one occasion he passed urine involuntarily. On the morning of March 14 there was noted for the first time some impairment of the percussion note over the left back below the angle of scapula. Numerous fine and coarse moist râles were heard over this area at the end of inspiration, and just below the angle of the scapula distant tubular breathing was audible. On this day lumbar puncture was performed for the second time, and 10 cc. of cloudy fluid were obtained. Cover slip preparations from the sediment showed a few intra-cellular biscuit-shaped organisms, decolorizing by Gram, and quite numerous lanceolate diplococci, only a few of which were intra-cellular, and all staining by Gram. Cultures made on blood serum from this fluid showed a pure growth of *Diplococcus meningitidis*, but no growth of *Diplococcus pneumoniæ*, which was also apparently present in the cover slip preparations. Blood cultures were made on the same day, and in all the media a pure growth of a diplococcus was obtained, which showed the cultural and staining reactions characteristic of the *Diplococcus pneumoniæ*. On the following day signs of consolidation of the left lower lobe became more pronounced. The respirations continued rapid and there was a definite respiratory grunt. The mental condition remained unaltered. Rigidity of the neck persisted. The restlessness, which had somewhat abated, now became more marked. At no time was there any eruption noted upon the skin. On March 19 it was noted that the skin was tinged yellow. Marked cyanosis, with great respiratory distress, developed on March 21, and death occurred rather suddenly at 11 a. m.

*An autopsy* was not performed.

The probable association of meningococci and pneumococci in the cerebro-spinal exudate makes this case one of peculiar interest. The case occurred during an epidemic of cerebro-spinal fever, and the history and clinical features, together with the demonstration of organisms, morphologically identical with the *Diplococcus meningitidis*, in the cerebro-spinal fluid, make it quite certain that the meningitis was primarily of meningococcic origin. Lobar pneumonia developed on the seventh day and the *Diplococcus pneumoniæ* was isolated from the cir-

culating blood. The demonstration of encapsulated, lanceolate, Gram-staining diplococci in the cerebro-spinal fluid, which also contained meningococci, as previously shown by culture, indicated that the *Diplococcus pneumoniæ* had invaded the meninges, which were already the seat of a meningococcus infection.

Case 7.—Lobar pneumonia (rt. upper); meningitis; acute ulcerative endocarditis of aortic valves.

Med. No. 9862. Male, æt. 52.

Admitted May 6, 1899. No history could be obtained beyond the fact that the present illness began eight days before admission with pain in the right side of the chest.

*Physical Examination.*—The patient was in a semi-conscious condition upon admission. His temperature was 99.2° F.; pulse 108; respiration 32, somewhat labored. The pupils were markedly dilated, equal, and apparently inactive. The tongue was protruded in the median line, slightly coated. The remains of a herpes were present upon the lips. Examination of the chest revealed signs of consolidation of the right upper lobe. The heart sounds were regular, but rather faint, and a fairly well-marked murmur of aortic insufficiency was audible. There was well-marked rigidity of the neck, the arms were held stiffly flexed on the chest, and the thighs and legs were also flexed. The patient resisted attempts to extend the extremities. Kernig's sign was bilaterally positive. Both knee jerks were present, the right slightly increased. There was slight ankle clonus on the right side. On the following day lumbar puncture was performed and about 5 cc. of perfectly clear, limpid fluid were obtained. Smears and cultures made from this fluid gave negative results. On the following day the patient's temperature fell to normal and remained there during May 9 and 10, rising to 100° F. the evening of May 11. On May 9 it was noted that the patient seemed much brighter and responded to questions. There was still marked rigidity of the neck and shoulder muscles, however, and Kernig's sign remained positive. The lung signs continued unchanged, though the patient's general condition seemed decidedly improved. Lumbar puncture was performed for the second time on May 10, 30 cc. of crystal-clear fluid being obtained. Smears and cultures from this fluid were entirely negative. The patient's condition continued the same until May 12, when the temperature began to rise gradually, reaching 105.4° F. at 4 a. m. on May 13. On this day a general tremor was noticed. There was an ankle clonus and the reflexes were generally increased. The patient was still conscious and responded to questions. Lumbar puncture was now performed for the third time and about 10 cc. of turbid fluid were obtained. Cover slip preparations from the sediment of the centrifugalized specimen showed several biscuit-shaped diplococci. Cultures made from this fluid were entirely negative. Upon

the same day blood cultures were taken, which yielded a pure growth of diplococci exhibiting all the morphological and cultural characteristics of the *Diplococcus pneumoniæ*. Mice inoculated with these organisms died in 24 hours, and from the blood the *Diplococcus pneumoniæ* was recovered. No especial change was noted in the patient's condition during the days of May 13 and 14. The temperature was irregular, ranging between 105.5° F. and 101.5° F. During the evening of May 14 the pulse gradually grew weaker, and the patient died at 10 p. m.

*Autopsy No. 1362.*—Anatomical diagnosis: "Acute lobar pneumonia (gray hepatization and gangrene); acute ulcerative endocarditis of the aortic valve; cardiac hypertrophy and dilatation; acute meningitis; cloudy swelling of the viscera; chronic diffuse nephritis; general arterio-sclerosis."

*Brain.*—"Over both sides of the cerebellum, at its lateral margin, there are small areas showing a collection of pus beneath the meninges. A similar small collection of purulent exudate is present in the Sylvian fissure. The dura on the right side shows a few hæmorrhages on its inner surface. The cord shows no macroscopic lesions, although the spinal fluid is turbid."

*Bacteriological Report.*—In the cultures made from the heart's blood, the valve vegetations, pericardial exudate, kidney, spleen, lung abscess, meningeal exudate, and spinal fluid, there developed a pure growth of *Diplococcus pneumoniæ*.

Case 8.—Lobar pneumonia (rt. lower); meningitis; pneumococcic panophthalmitis; acute ulcerative endocarditis of the mitral and aortic valves.

Med. No. 10,548. Male, æt. 37. Occupation, laborer.

Admitted November 5, 1899, complaining of shortness of breath.

*Family and past history* were unimportant.

The patient was in no condition to give a clear account of his present illness. He had been feeling badly for about six weeks. Some 16 days previous to admission he began to have shortness of breath and a cough with bloody expectoration. He gave a history of having been swollen two weeks prior to his admission, and had had frequency of micturition and severe headaches.

*Physical Examination.*—The patient appeared moderately ill on admission. The temperature was 98.8° F.; pulse 108; respirations 32. He had a severe cough and tenacious bloody sputum. There were signs of consolidation of the right lower lobe. The area of cardiac dulness was increased, and there were signs of insufficiency of both aortic and mitral valves. During the next seven days the patient's condition remained unchanged. The temperature was intermittent, not rising above 100.8° F. until during the night of November 12, when it rose suddenly to 105.8° F. With this sudden rise in temperature the patient became comatose, would not respond to questions, and there was twitching of the muscles of the right hand. The pupils were equal, but quite small, and did not respond to light. There was no stiffness of the neck. The reflexes were much exag-

gerated. Kernig's sign was bilaterally present. The spleen was enlarged and there seemed to be tenderness in the splenic region. During the day of November 13 the patient's mental condition became decidedly brighter, and by 5 p. m. he responded clearly to questions. He continued in this condition, with general stiffness of the muscles of the extremities, positive Kernig's sign, and fever, for three days. On November 15 lumbar puncture was performed and 15 cc. of slightly turbid fluid were withdrawn. Smears made from this fluid showed many lanceolate diplococci, and cultures subsequently yielded a pure growth of the *Diplococcus pneumoniæ*. On November 16 a purulent discharge from the right eye developed. Smears from this discharge showed organisms having the staining and morphological characteristics of the *Diplococcus pneumoniæ*. On the same day cultures were made from the circulating blood, but with negative result. The patient's condition grew gradually worse. There were no convulsions, and the mental condition remained clear until two hours before death, which occurred at 2 a. m., November 16.

*Autopsy No. 1442.*—Anatomical diagnosis: "Purulent cerebro-spinal lepto-meningitis; acute purulent panophthalmitis; acute ulcerative endocarditis of the aortic and mitral valves; acute endocarditis; cardiac hypertrophy and dilatation; arterio-sclerosis of the aortic and coronary arteries; thrombosis of the superior sagittal sinuses; pulmonary infarct; lobular pneumonia and acute pleurisy; splenic infarct; chronic diffuse nephritis."

*Brain and Spinal Cord.*—"The dura is adherent to the cranium. The superior sagittal sinus in its anterior portion contains a number of blood clots and pacchyonian granulations, which project into the lumen of the sinus. On the ventral surface of the brain the arachnoid is raised from the underlying pia by a considerable amount of pus. On incision through the arachnoid the pus is found to have a depth of 2 mm. over the optic chiasm, completely concealing that structure. The pus follows the course of the lateral cerebral fossæ, concealing the blood vessels. On the lateral surface of the brain there is pus in the larger sulci, being more noticeable in small, irregularly distributed areas. These areas are also seen over the superior surface of the brain.

"The dura of the spinal cord upon its external surface is normal and unattended with congestion of the blood vessels. The internal surface of the dura appears smooth and of a faint pink color. The subarachnoid space over the dorsal surface of the lumbar swelling is in places filled with yellowish pus. The posterior columns of the dorsal cord are of a yellowish-green color, due to the same exudate. In the thoracic portion this pus is thick and compact, concealing the cord. The same condition is present in the cerebellar portion. The blood-vessels of the pia are, in parts, much injected."

*Bacteriological Report.*—Cultures from lungs, cerebral meninges, heart's blood, vegetations of the aortic and mitral valves, and from an abscess in the mitral valve all yielded a growth of the *Diplococcus pneumoniæ*.

Case 9.—Lobar pneumonia (rt. lower); pneumococcus meningitis.

Med. No. 10,791. Male, æt. 62. Occupation, ship's pilot.

Admitted January 15, 1900, complaining of pain in abdomen.

*Family history and past history* were unimportant.

*Present Illness.*—On January 2, 13 days before admission, the patient had a shaking chill and pain in the right side of the chest. From that time up to day of admission he had been in bed with fever, cough, and pain in the right side of abdomen. There had been very little expectoration.

*Physical Examination.*—On admission the temperature was 100.4° F.; pulse 100; respirations 28. Examination of the chest showed that there was flatness below the 3d rib over the right front, with definite cracked-pot sound at the lower margin of the lung. There was also flatness at the right base behind and definite tubular breathing at the angle of the right scapula. On the day after admission the patient's temperature fell to normal and did not rise above 99.2° F. until the evening of January 17. On January 16 the general condition seemed somewhat improved. The pulmonary signs, however, remained the same, except that there was some impairment over the left upper front and axilla, with harsh breath sounds over this region. On January 17 the patient's condition rapidly grew worse, and he died at 10 p. m. At no time were there any symptoms or signs which pointed to meningeal involvement. The leucocytes ranged between 15,000 and 18,000.

*Autopsy No. 1470.*—Anatomical diagnosis: "Lobar pneumonia (lower lobe of right lung); small areas of gangrene; fibrinous pleurisy; lobular pneumonia of the left lung; fibrous myocarditis; old valvular endocarditis; fatty liver; acute splenic tumor; cloudy swelling of the kidneys; general arterio-sclerosis; fibrinous basilar meningitis."

*Brain.*—"Over the base, as far forward as the anterior perforated space below the fissure of Sylvius, and below the surface of the cerebellum, is a fibrinous exudate. This exudate also extends somewhat over the convexity of the brain. The cerebellar vessels are considerably congested."

*Cultures* from the lung, pleural exudate, and meninges yielded a growth of the *Diplococcus pneumoniæ*.

Case 10.—Lobar pneumonia (rt. upper and middle); meningitis.

Med. No. 12,368. Male, æt. 38. Occupation, ship builder.

Patient was a marked alcoholic, with a history of typical onset of pneumonia four days before admission. Anamesis otherwise unimportant.

*Physical Examination.*—On admission the patient was rational, but appeared quite sick. There were signs of consolidation of the upper and middle lobes of the right lung. His condition gradually became worse, until on the night of the sixth day the respirations became irregular and shallow, and finally the patient became intensely cyanotic. The pulse continued fairly good, artificial respiration was employed, and after several minutes spontaneous respiration was resumed. Following this attack the respirations became Cheyne-Stokes in character. At this time the pupils

were unequal, the right being larger than the left, and there was external strabismus of the left eye. Kernig's sign was well marked. Definite convulsive movements occurred at intervals, the extremities and back becoming rigid with the head retracted, and clonic movements occurred in the arms. At 3.30 p. m. lumbar puncture was performed and 25 cc. of turbid fluid were obtained. Cover slip preparations from the centrifugalized sediment showed very few leucocytes, but numerous encapsulated lanceolate diplococci. Cultures from this fluid subsequently yielded a pure growth of the *Diplococcus pneumoniæ*. Slight convulsive movements of the extremities recurred at intervals until 9 p. m., when there was a short general convulsion, the head being drawn back and the arms and legs flexed. Following this there were no further convulsions, the rigidity disappeared, and the respirations became regular again. The strabismus also disappeared, but the right pupil continued larger than the left. Pulmonary œdema now gradually developed, the heart's action became weaker, and death occurred at 11 p. m.

*Autopsy No. 1656.*—Anatomical diagnosis: "Acute lobar pneumonia of the right upper and middle lobes; acute fibrinous pleurisy; acute fibrinopurulent meningitis; acute splenic tumor."

*Brain.*—"The dura is adherent only at the site of the pacchyonian granulations. Upon the surface of the hemispheres the soft meninges have an opaque, grayish-yellow appearance, due to the presence of a thick exudate, which in places gives them a thickness of 15 mm. This exudate is most abundant over the convex surface of the frontal lobes, but is abundant everywhere. There is a moderate amount of exudate upon the cerebellum, with very little at the base of brain. The velum interpositum is infiltrated with a similar exudate. The ventricles contain a turbid yellow fluid."

Case 11.—Primary pneumococcic polyarthritis; meningitis; no lobar pneumonia.

Med. No. 12,547. Male, æt. 55. Admitted February 13, 1901, and died February 15, 1901.

The patient was irrational on admission to the hospital, and the history was obtained from his wife.

The *family and past history* were unimportant.

*Present Illness.*—For four or five weeks prior to admission the patient had suffered with swelling and soreness of his knees, especially the right knee. On Sunday, February 10, the patient had a slight chill in the afternoon and another during the night. He felt fairly well the next day. On Tuesday, the 12th, he complained of pain in the lower left side and in the right axilla. He was delirious Tuesday night and Wednesday, the day of admission to the hospital. He had had no cough nor expectoration and no dyspnœa.

*Physical Examination.*—The patient was a sparsely nourished colored man, very apathetic, lying with the head rotated toward the left shoulder. The eyes were negative.

Both lungs were clear except for a slight impairment of the percussion note with enfeebled breath sounds below the left clavicle down to the third rib. There were no râles and no tubular breathing.

The wrists, ankles, and knees were swollen and very tender.

On the following day the neck was found to be very rigid. Kernig's sign was not tested for because of the existing arthritis. There were now signs of pneumonic involvement of the right lower lobe.

The leucocytes were 10,000; the temperature was 105° F.; pulse 92.

Lumbar puncture was performed on the 14th and 20 cc. of turbid, pale yellow fluid removed. The fluid contained numerous leucocytes and diplococci, having the morphology and staining properties of the *Diplococcus pneumoniæ*. Fluid aspirated from the right knee joint was quite similar in appearance to the cerebro-spinal fluid, containing leucocytes and the *Diplococcus pneumoniæ*.

Kernig's sign was now found to be positive.

The patient died February 15, two days after admission.

A blood culture taken February 14 showed subsequently a pure growth of the *Diplococcus pneumoniæ*, as did cultures from the cerebro-spinal fluid and fluid aspirated from the right knee joint.

*Autopsy No. 1677.*—Anatomical diagnosis: "Acute purulent lepto-meningitis; acute purulent arthritis; acute broncho-pneumonia; hæmorrhagic pacchymeningitis; chronic arthritis deformans; healing round ulcer of stomach; arterio-sclerosis; chronic pulmonary tuberculosis; chronic bilateral pleuritis; œdema of the lungs."

*Brain.*—"Over the surface of the cerebral hemispheres the sulci are filled with greenish, purulent exudate, which extends over the base of the brain, optic chiasm, the lobes of the cerebellum, and to a certain extent down around the medulla. Cutting through the corpus callosum, the meninges around the cerebral peduncles are found infiltrated with a purulent exudate."

The spinal cord was not examined.

Case 12.—Lobar pneumonia (rt. upper); acute ulcerative endocarditis of the aortic and tricuspid valves.

Med. No. 15,748. Male, æt. 42. Occupation, clerk.

Admitted June 2, 1903, complaining of cough and weakness.

*Family history* unimportant.

*Past History.*—The patient had had pleurisy twice and was subject to frequent colds. He had had frequent night sweats. He was accustomed to get up once or twice each night to urinate and his ankles were somewhat swollen. He had been an immoderate drinker of whiskey and beer.

*Present Illness.*—For several days prior to admission the patient had been feeling weak and tired, with a poor appetite. On May 30 he had a chill, followed by a drenching sweat, and subsequently a severe cough with non-sanguineous expectoration developed.

*Physical Examination.*—There were signs of early consolidation of the right lower lobe on admission, and these gradually became outspoken. There was marked tremor of the hands and arms, and the patient complained of pain in the right shoulder joint. He gradually became irrational, and marked rigidity of the neck with positive Kernig's sign developed. A pericardial friction rub and loud diastolic murmur now appeared, and the pulse became collapsing. Six days after admission the right ankle joint became red and swollen and fluid aspirated from it proved to contain the *Diplococcus pneumoniæ*. A lumbar puncture was performed June 8, but the fluid obtained was clear and culturally showed no organisms. The leucocytes upon admission were 13,000; June 4, 10,400; June 5, 8100; June 9, 9100; June 7, 10,200; and upon the day of death, June 9, 10,300. A blood culture performed June 8 revealed the presence of the *Diplococcus pneumoniæ* in the blood. The temperature curve was very choppy, ranging from normal to 105.5° F. The respirations were from 30 to 40 per minute, and the pulse 120 to 140. The patient died June 9, seven days after admission.

*Autopsy No. 2119.*—Anatomical diagnosis: "Lobar pneumonia with gray hepatization of right lung; chronic adhesive pericarditis; acute endocarditis with ulceration of the aortic valve; acute tricuspid endocarditis; fatty myocarditis; atheroma of aorta and coronaries; cirrhosis of the liver; chronic interstitial pancreatitis; fatty degeneration of the kidneys; acute splenic tumor; acute arthritis of the right ankle joint; acute lepto-meningitis."

*Brain.*—"The superior longitudinal sinus is filled with a dark red clot. The surface of the brain is rather pale. The sulci are filled with a purulent exudate and the large pial vessels are filled with clots. The cranial nerves, the pia covering the pons, medulla and posterior part of the cerebellum, is covered with a purulent exudate. The foramen of Majendie is closed by this exudate, and the fluid pressed from the fourth ventricle is definitely purulent."

The cord was not removed. Cultures from the exudate upon the cerebral meninges revealed the *Diplococcus pneumoniæ*, as did cultures from the vegetations upon the aortic valves.

Case 13.—Pneumonia (lt. lower); no clinical signs of meningitis; acute purulent lepto-meningitis found post-mortem.

Med. No. 15,967. Male, æt. 24. Negro. Occupation, laborer.

Admitted July 30, 1903, complaining of pain in side. Died August 4, 1903.

*Family and past history* are unimportant.

*Present illness* began nine days before admission with a shaking chill, headache, anorexia, fever, cough, and pain in left side.

*Physical Examination.*—On admission, July 30, the only positive findings were signs of lobar pneumonia in the left lower lobe. The patient was conscious and rational. The heart was noted as clear of abnormal sounds.

During the patient's stay in the hospital there were apparently no signs whatsoever of meningeal involvement. On the day of death it was noted that the patient was unconscious, but not delirious, and lay with the hands held upon his head. No muscular rigidity, cervical retraction, vomiting, or Kernig's sign were noted. No lumbar puncture was performed.

The leucocytes numbered 9600 upon admission and were 30,000 August 3. Blood culture was negative.

The temperature ranged from 102° F. to 104.5°F. The pulse ranged from 100 to 144.

*Autopsy No. 2149.*—Anatomical diagnosis: "Lobar pneumonia (gray hepatization); acute purulent pleuritis; acute fibrino-purulent pericarditis; cloudy swelling of heart, liver, and kidneys; acute splenic tumor; acute purulent lepto-meningitis."

*Brain.*—"The superior longitudinal sinus is filled with a dark red clot. The surface is rather pale. The sulci are filled with a purulent exudate. The larger pial vessels are filled with clots. The injection of the brain is most marked in the larger vessels. The cranial nerves, the pia covering the pons, medulla, and the posterior part of the cerebellum is covered with the same kind of exudate. The foramen Majendie is closed by this exudate, and the cerebro-spinal fluid pressed from the fourth ventricle is definitely purulent."

Case 14.—Lobar pneumonia (rt. lower); acute ulcerative endocarditis of the aortic valves; meningitis.

Med. No. 16,559. Male, æt. 42. Occupation, laborer.

Admitted January 2, 1904, complaining of pain in the right side.

*Family history* was unimportant.

*Past History.*—The patient had been leading a vagabond existence, sleeping in a hay-loft 10 days prior to admission.

*Present Illness.*—The onset of the present illness was two days before admission, with a shaking chill, sharp, cutting pain in the right side, headache, and loss of appetite.

*Physical Examination.*—The patient gradually developed out-spoken signs of lobar pneumonia of the right lower lobe, with typical fever pulse and leucocytosis. On the 10th day of the disease the temperature fell from 104° F. to 100.5° F., and the general improvement of the patient's condition seemed to indicate the beginning of convalescence. The temperature, however, remained at 100° F. during the next two days, and then on the 13th day of the disease rose to 102° F. From this time until the patient's death the temperature curve was irregular and choppy, with a maximum of 105° F. and a minimum of 100.5° F., and the patient was subject to drenching sweats. On the 17th day of the disease a loud aortic diastolic murmur developed, and the pulse became collapsing in quality. On the same day rigidity of the neck and a suggestion of Kernig's sign were noted, both of which grew more marked before death. A lumbar puncture was done on the day of death and a turbid fluid containing numerous diplococci was

obtained. Cultures from this fluid revealed the *Diplococcus pneumoniæ*. Three days before death the patient became drowsy and complained of headache. A low muttering delirium gradually developed, and patient sank into unconsciousness and died on January 17, 18 days from the onset of the illness. A blood culture taken on the day before death yielded a pure growth of *Diplococcus pneumoniæ*.

*Autopsy No. 2232.*—Anatomical diagnosis: "Acute lobar pneumonia with organization; acute ulcerative endocarditis of the aortic valves; infarction of the spleen and kidneys; acute fibrino-purulent cerebro-spinal meningitis."

*Brain.*—"On removing the brain a thick, greenish, fibrino-purulent exudate is found to cover the inferior surface of the cerebellum, pons, and medulla, extending deep into the sulci, covering the nerves as they pass out. The ependymal surfaces are greatly roughened and somewhat injected."

*Cord.*—"The vessels of the dura are deeply injected. The pia-arachnoid is densely infiltrated with an exudate similar to the greenish-white exudate noted above."

Case 15.—Very insidious onset of meningitis; discharging sinus over left buttock; no lobar pneumonia.

Med. No. 16,592. Female, æt. 53.

Admitted January 11, 1904, complaining of nervousness.

*Family and past history* were unimportant.

*Present Illness.*—About six months before admission (July, 1903) the patient began to feel badly, having headache and general languor. In August, 1903, she had a general convulsion with rolling of the eyes, cyanosis, biting of the tongue, and foaming at the mouth. Similar attacks occurred in September, October, and November, 1903. The patient remained in bed from August to October. In the intervals between attacks the patient was clear mentally and felt fairly well. During December, 1903, she seemed to improve and came from Virginia to Baltimore on Christmas Eve, but grew rapidly worse immediately after her arrival. During the summer the patient had had many boils on the legs, and one of these, situated upon the left buttock, developed into a large abscess which refused to heal. The patient had had no convulsions for four weeks prior to admission, but for several days before admission she was mentally confused, with difficulty in speech.

*Physical Examination.*—The patient was in a very nervous condition upon admission to the hospital. The eyes were wild and staring and the whole body was trembling constantly. Within two days the patient had grown mentally clear, and physical examination at this time revealed nothing beyond the discharging subcutaneous sinus over the left buttock. The patient was thin, but not emaciated. Upon the fifth day after admission she had four convulsions. During the first convulsion the whole body was at first rigid, relaxing gradually after two or three minutes. The

second attack followed in half an hour; both arms were tonically contracted, the right leg twitching tonically; the left was flaccid; the eyes and head were turned to the right. Two other convulsions occurred during the day, the first of these confined to the left side, and the second to the right side of the body. Plantar stimulation caused extension of the great toe on both sides (Babinski positive). Three more convulsions occurred upon the following day (February 13) and the patient became completely unconscious with slow and shallow respirations. The temperature rose to 102.5° F., the pulse rising from 80 to 104. There was no leucocytosis. The temperature fell to 99° F. upon the 17th; the pulse was 72 to 80; and from this date until February 24 the patient seemed to improve, regaining consciousness and becoming entirely rational. The ocular fundi were described as negative. A lumbar puncture, performed upon the 22d, yielded a clear fluid, which proved sterile upon the various cultural media. From February 24 the patient's condition grew progressively worse; she became irrational, frequently shrieking in terror at the sight of bugs and snakes, which, she said, filled the room. It was noted that the hallucinations were strongly suggestive of chronic alcoholism. Upon the 28th the patient had fallen into a stupor with stertorous respirations and cyanosis of the face. The temperature, which had remained about 99° F., rose on this day to 104° F., and subsequently the temperature curve was of the choppy, septic type. On February 1 a blood culture was taken and a pure growth of *Diplococcus pneumoniæ* was obtained. A lumbar puncture on February 3 revealed a turbid fluid which contained numerous leucocytes, but no bacteria were demonstrated in the stained preparations. Cultures, however, revealed a pneumococcus. The leucocytes were noted as 11,000 upon the 1st of February, as compared with 5000 upon admission. The patient had several general convulsions upon the 3d of February, and the respirations became typically Cheyne-Stokes in type. The rigidity of the neck was noted for the first time upon February 4. On February 2 an area of dulness, with tubular breathing, over the first and second left interspace in front, numerous moist râles at both axillæ and bases behind, with impairment of the note at both bases, were noted. A third lumbar puncture, performed February 5, yielded a very turbid fluid in which numerous leucocytes and diplococci were seen. The diplococci showed the cultural and staining characteristics of the *Diplococcus pneumoniæ*. The urine was rather scanty, the specific gravity averaged 1022; there was a trace of albumin and a few hyaline casts. The patient died February 5, 25 days after admission.

*Autopsy No. 2241.*—Anatomical diagnosis: "Chronic nephritis; slight arterio-sclerosis; fatty degeneration of the heart; partial atelectasis of the lungs; embolism of the pulmonary artery; propagated thrombosis of the pulmonary artery; infarction of the lung; acute cerebro-spinal meningitis; dropsy of the convolutions of the cerebrum; œdema of the meninges."

*Brain.*—"Very much congested. There are portions which are greatly enlarged and prominent. The pia over the cerebral hemispheres is ex-

tremely œdematous, and through the anterior portion of the cerebral hemisphere and over the base of the brain, particularly over the pons and about the optic chiasm, extending into the sides of the sulci and over the cerebrum, is an opaque, grayish-white exudate. The ventricles contain turbid dark fluid. The ependyma is opaque and roughened-looking. The vessels of the brain are somewhat tortuous and thickened."

*Spinal Cord.*—"The cord shows a slight roughening on the ventral surface, but no well-defined exudate, while on the dorsal side the pale exudate is quite well marked. There are numerous small, white, ragged-looking flecks in the surface of the pia."

No immediate connection was demonstrated at autopsy between the discharging sinus over the left buttock and the cerebro-spinal infection.

Case 16.—Lobar pneumonia (rt. and lt. lower) with normal convalescence; late onset of meningitis; acute ulcerative endocarditis of the aortic valves.

Med. No. 16,805. Male, æt. 65. Occupation, cook.

Admitted March 4, 1904, complaining of cough and weakness.

*Family and past history* were negative.

*Present Illness.*—The patient gave a typical history of acute pneumonia with chills, sweats, cough with blood-stained very tenacious sputum.

*Physical Examination.*—The patient showed well-marked signs of consolidation at the bases of both lower lobes. The course of the disease was typical of pneumonia, with leucocytes reaching 23,000 and temperature averaging 102.5° F., falling by crisis on the eighth day. The heart sounds were noted as normal during the fastigium. The patient seemed to have entered upon a normal convalescence and for eight days the temperature was normal, the patient being up in a wheel chair. The right back had apparently not quite regained its normal resonance. On the 18th day after admission the patient had a chill and the temperature went up to 101° F. From this day until death the temperature ran a typically septic course with sudden falls of as much as 6°. Chills and sweats were frequent. On the 21st day systolic and diastolic murmurs were noted at the apex, and the relative cardiac dulness had increased in size. The lungs at this time showed no new involvement. The right base was persistently dull. On the 24th day of the disease the patient gradually lost consciousness and slight rigidity of the neck was noted. There was no Kernig's sign. The eyes were turned to the left and there was slight divergent strabismus; the pupils were equal. The diastolic murmur grew very loud and the pulse became markedly collapsing. A lumbar puncture was performed on the 25th day of the disease and 15 cc. of turbid fluid were obtained which contained innumerable diplococci. Cultures from this fluid revealed the *Diplococcus pneumoniæ*, as did cultures from the blood, taken on the same day. The temperature rose to 106.5° F. at 4 p. m., and the patient died on the 25th day of his illness.

*Autopsy No. 2273.*—Anatomical diagnosis: "Organizing lobar pneumonia of the right lung; terminal lobar pneumonia of both lungs; acute ulcerative endocarditis of the aortic valves; acute splenic tumor; sero-purulent meningitis of the spinal cord; arterio-sclerosis; slight chronic nephritis."

*Spinal Cord.*—"On being exposed shows distension of the dura. A turbid fluid is removed from this distended cavity. The spinal cord itself shows some hyperæmia and the veins are very tortuous. There is a small amount of opaque white exudate over the dorsal surface which, however, is very inconspicuous. It is present in patches over the dorsal and lumbar parts."

*Brain* not examined.

Case 17.—Caries of teeth; infection of antrum of Highmore and sphenoid sinuses; meningitis; no lobar pneumonia.

Med. No. 17,759. Male, æt. 20. Occupation, steamship steward.

The patient was admitted November 3, 1904, in an irrational condition, and died eight hours after admission.

The history obtained from the ship's surgeon was as follows: Three days before admission the patient began to complain of pain in right arm, right side of head, and right hypochrondium. Three weeks before he had had slight conjunctivitis with slight keratitis, which had persisted in spite of treatment. He had had fever constantly for three days prior to admission, though remaining perfectly clear mentally up to the afternoon before admission, when jaundice developed and the patient grew actively delirious. There were no convulsions. At 10.30 a. m. on the day of admission it was noted that the patient seemed extremely ill and was irrational. There was no strabismus, but there were sudden twitching movements of both eyeballs. A purulent conjunctivitis was present in the right eye and the lower lid was much thickened and inflamed. There was definite jaundice of the entire body. The muscles of the neck, arms, and legs were not spastic and the knee kicks were not exaggerated. The heart and lungs presented no physical abnormalities. The temperature was 106° F.; pulse 124; respiration 24; leucocytes 62,500. A blood culture taken at 12.30 p. m. subsequently yielded a pure growth of the *Diplococcus pneumoniæ*. At 12.30 p. m. the patient was quite delirious, holding his hands to the back of the head. The neck had become quite rigid, and a definite Kernig's sign was present in both legs, which were held quite stiffly. The arms were not stiff. At times there was marked internal strabismus of the right eye and muscular twitching of both eyeballs was constant. Priapism was present. About 30 cc. of greenish-yellow, very turbid fluid was removed by spinal puncture at 3.30 p. m. Microscopically, the fluid contained numerous leucocytes and diplococci. Cultures revealed the *Diplococcus pneumoniæ*.

*Autopsy No. 2407.*—Anatomical diagnosis: "Caries of teeth; infection of the antrum of Highmore and sphenoid sinuses on the right side; gen-

eralized lepto-meningitis; acute splenic tumor; parenchymatous degeneration of the liver and kidneys."

*Brain.*—"Shows over its surface everywhere a thick, greenish-yellow exudate, which is soft and semifluid in character. This is not only beneath the pia, but also upon its surface. The dura, which remains adherent to the skull, is thickly covered with the same yellow exudate. The exudate is most abundant over the frontal portions of the cerebral hemispheres. It extends also into the longitudinal fissures and is found over the base of the brain, extending over both surfaces of the cerebellum, and, to a less extent, over the pons and medulla. The cerebral ventricles contain an excess of fluid. The lining of the ependyma is smooth and clear. The choroid plexuses are not involved. The patient had complained of pain in the right ear and had presented at the same time a suppurative conjunctivitis of the right side. The orbit, middle, and inner ear on the right side were examined, but found normal. The sphenoid sinuses and antrum of Highmore on the right side were opened into and found to contain a quantity of greenish pus which ran out of these cavities. The lining mucosa was greatly swollen and red. The examination of the mouth showed the presence of caries in both upper and lower molars on the right side and an extremely foul condition of all the teeth and mucosa."

Case 18.—Terminal infection of the meninges with the *Diplococcus pneumoniæ*.

Med. No. 17,859. Female, æt. 37.

Admitted December 1, 1904, complaining of dropsy.

*Family and past history* were negative.

*Present Illness.*—For four or five months prior to admission the patient had suffered with headaches, failing vision, shortness of breath, and swelling of the ankles, which gradually developed into anasarca. She was very drowsy and œdematous upon admission, and rapidly sank into unconsciousness.

*Physical Examination* revealed an emaciated woman with marked œdema of the arms, legs, and back. She was unconscious, and while there was no retraction of the neck, it was held very rigidly. The arms were rather stiff, but the legs were flaccid and there was no Kernig's sign. Respirations were slow, 12 to the minute; pulse could not be counted at the wrist, but at the apex by stethoscope was 92. The temperature was 96° F. The lungs showed signs of broncho-pneumonia. The heart was clear. There were 2,856,000 erythrocytes; 3580 leucocytes; 33 per cent hemoglobin. A lumbar puncture revealed a clear fluid, which was under normal tension. No bacteria were demonstrable in the stained fluid, but cultures showed an organism with the typical morphology and staining reactions of the *Diplococcus pneumoniæ*.

The patient died the day following admission.

*Autopsy* not obtained.

Case 19.—Lobar pneumonia (rt. lower); subcutaneous emphysema following thoracentesis; meningitis.

Med. No. 18,576. Female, æt. two years.

Admitted June 24, 1905, with the complaint of cough and fever.

*Family history and past history* unimportant.

*Present Illness.*—Fifteen days before admission the child began to cry a great deal, seemed feverish, and had a constant cough. The entire body seemed very sensitive to pressure, the child crying loudly when moved.

*Physical Examination.*—On admission there were out-spoken signs of acute lobar pneumonia in the right lower lobe. To exclude the possibility of empyema an exploratory thoracentesis was done, but no fluid found. Four days after the aspiration a subcutaneous emphysema, extending from the clavicle to the groin on the right side, developed. On the 27th the patient had a violent general convulsion lasting 20 minutes. There was a constant bilateral internal strabismus, with spasmodic downward jerkings of both eyes. No Kernig's sign was present, but there was a marked general rigidity of the muscles. The head was not retracted. The child grew rapidly worse, and few hours before death it was noted that the neck was not especially stiff. The arms, however, were very stiff, and the patient moved them convulsively from time to time. The legs were held very rigidly. There was no Kernig's sign at any time. Before death there developed a well-marked ptosis of the left eyelid and the left eye did not move. The rhythmic, spasmodic, downward jerking of the right eye was still in evidence. The signs of lobar pneumonia persisted over the right lower lobe. The temperature was 106.5° F.; pulse 180; leucocytes 10,400. About 10 cc. of cerebro-spinal fluid was removed by lumbar puncture on the day of death. Interspinal pressure was 450 mm. of the fluid, and the fluid contained many leucocytes and extracellular diplococci, which culturally proved to be the *Diplococcus pneumoniæ*.

No autopsy.

Case 20.—Meningitis due to the *Diplococcus pneumoniæ;* no lobar pneumonia.

Med. No. 18,961. Male, æt. three months.

Admitted October 18, 1905, with the complaint of fever and spasms.

*Family history and past history* not important.

*Present Illness.*—Two weeks before admission the patient developed a cough which persisted until admission. Six days before being brought to the hospital the child became fretful, crying when moved as if in great pain. On this day he had a spasm, the arms becoming stiff, head thrown back, and eyes rolling from side to side.

*Physical Examination.*—The baby was well-nourished, with no evidence of rickets. There was no discharge from ears and no mastoid tenderness. The anterior fontanel was bulging. Respirations were 11 to the minute. The neck and arms were held stiffly, but there was no Babinski's or Kernig's sign. Numerous moist râles were heard over both lungs. No tubular

breathing; no dulness. There was a moderately loud blowing systolic murmur at the apex of the heart. The leucocytes numbered 23,000. On the day of admission the patient had four convulsions and during the next 24 hours had several more. He rapidly sank into complete unconsciousness and died in a convulsion on the second day after admission. The temperature on admission was 106° F., falling in two hours to 103° F., and in 14 hours was 99.5° F., rising, however, within eight hours to 103° F.—presenting a typical ragged septic curve. The pulse was constantly high, from 160 to 180, and the respirations rose to 60 per minute. A lumbar puncture performed on the day of death revealed a turbid fluid under pressure of 380 mm. of the fluid. Microscopically, the fluid was filled with diplococci staining by Gram. Some of the organisms had a well-marked suggestion of a capsule in the Gram stain. Three glycerine agar plates were made from the fluid, but they remained sterile. The bacteriological diagnosis was *Diplococcus pneumoniæ*.

*Autopsy No. 2606.*—Anatomical diagnosis: "Acute suppurative cerebral lepto-meningitis; acute meningitis of the cord; cloudy swelling of the viscera; fatty degeneration of the liver."

*Brain.*—"On removing the skull cap one finds within the dura mater an exudate of considerable amount, purulent in character and containing large flakes of fibrin. On removing the brain this exudate is found to be thickest and heaviest over the frontal lobes, in the sulci, and in the fissures between the frontal and parietal lobes. The exudate forms a thick, fibrino-purulent layer especially marked along the vessels. The base of the brain is somewhat affected, although the exudate is not as great in amount as over the cortical surfaces. The ventricles contain a small amount of slightly bloody fluid. On examination of the cranial cavity the exudate is found to be most marked in the right frontal fossa and over the cribriform plate. On examination the external and middle ear and the sphenoid sinuses show no evidence of suppuration. There is no sign of external injury on the scalp.

"On opening the spinal canal there is found to be a thick, purulent, slightly hæmorrhagic exudate which lies exterior to the dura mater of the cord. There is very marked injection of the vessels of the pia mater and a slight cloudiness through that membrane, but no definite exudate in the pia mater. The extradural exudate is well marked as far as the cauda equini."

Case 21.—Lobar pneumonia (lt. upper and lower); acute onset of meningitis.

Med. No. 20,556. Male, æt. 50.

Admitted December 27, 1906, complaining of cough and pain in the side.

*Family and past history* were negative.

*Present Illness.*—Began with a sudden and typical onset of pneumonia.

*Physical Examination.*—Revealed out-spoken signs of consolidation of the left lower lobe. The heart rate was 128 to the minute; temperature

104° F.; leucocytes 9000. On the fourth day after admission the patient became irrational and his condition was noted as markedly worse. The temperature rose rapidly from 102° F. to 104° F. and at first the pulse was relatively slow, 104 to the minute, rising, however, as death approached to 150 to the minute. The leucocytes were 34,000 on the day of death. No stiffness or retraction of the neck was noted, but there was a positive Kernig's sign in both legs. A slight divergent squint was noted in the left eye. The heart remained clear. Fifteen cubic centimeters of very turbid spinal fluid, removed by lumbar puncture eight hours before death, showed innumerable encapsulated Gram-staining diplococci. The patient died on the sixth day after admission and the eighth of the disease.

*Autopsy No. 2825.*—Anatomical diagnosis: "Acute lobar pneumonia with consolidation of the upper and lower lobes of the left lung; acute fibrino-purulent meningitis affecting brain and cord; cloudy swelling of viscera; acute splenic tumor; chronic adhesive pleuritis."

*Brain.*—"On removing the dura from the cortex of the brain, there is found to be an exudate of greenish yellow color, infiltrating the pia over the frontal portions of the cerebral hemispheres, but extending also to a lesser degree over the upper and parietal surfaces of the brain. On removing the brain it is found that this exudate extends over the whole base of the brain, the cord, the medulla, the pons, optic chiasm, fissures of Sylvius, as well as the posterior part of the cerebellum, being thickly covered with the same greenish exudate. All the cranial nerves and blood vessels are embedded in this material. On incision into the brain it is found that the exudate extends far down into the sulci. No definite gross change can be seen in the cortical substance. The ventricles contain a quantity of turbid, greenish fluid, in which float flakes of fibrin. The choroid plexuses are masked by accumulations of this exudate. The fourth ventricle is filled with the same purulent exudate. The substance of the cerebellum and hemispheres shows no gross change, nor does that of the pons or medulla. In sections across the base of the brain the exudate may be traced into all crevices, but otherwise there is no alteration."

*Spinal Cord.*—"There is abundant fat outside the dura of the cord. The blood vessels are distended with blood. The pia of the cord is found to be thickly infiltrated, especially over the dorsal surface, with a greenish exudate similar to that seen in the brain. On opening the dura from the ventral aspect it is found that this exudate is quite as abundant there as on the dorsal side.

Case 22.—Lobar pneumonia (lt. lower and rt. upper); sero-purulent lepto-meningitis.

Med. No. 21,461. Female, æt. 65. White.

Admitted August 13, 1907. Died August 28, 1907.

The patient was brought to the hospital unconscious, with the following history given by her son:

Five days before admission to the hospital the patient complained of headache, which grew gradually worse, and she remained in bed. She gradually sank into unconsciousness two days before admission, and had remained unconscious ever since. There were no convulsions and no delirium prior to admission.

*Physical Examination.*—The patient was comatose and did not answer questions. The lungs and heart were clear of abnormal physical signs. There was no discharge from ears and no tenderness over mastoids. The neck was a trifle stiff. Knee kicks were not obtained; no positive Kernig's sign.

The day following admission the patient became brighter and talked to those about her, answering questions rationally. For seven days following the patient seemed to gradually improve, though at times distinctly irrational. She continually asked for water and for an ice cap for her head. On August 21, two weeks after admission, the patient became noisily delirious and complained of pain in the left chest. The respirations were 40 to minute. On August 25 it was noted that the patient was conscious. There was a slight external strabismus, the neck was quite rigid, and the patient complained of pain in the top of her head. The left side of the body seemed rather flaccid, though there was no difference in the reflexes of the two sides. On August 28 signs of lobar pneumonia of the left lower lobe were first noted. A lumbar puncture was performed on August 26, but the resulting fluid was negative.

The leucocytes on admission were 10,100 and on the day of death 12,600.

The temperature on admission was 99.5° F. and did not go above this point for the following five days. It then became irregular, markedly remittent in type, and ranged between 99° F. and 102° F. until three days before death, when it became subnormal and remained so until the end.

*Autopsy No. 2927.*—Anatomical diagnosis: "Lepto-meningitis (sero-purulent; acute and organizing); hæmorrhage into exudate; internal hydrocephalus; lobar pneumonia; submaxillary lymphadenitis; atheromatous ulceration of aorta; arterio-sclerosis, especially marked in coronaries; acute nephritis."

*Brain.*—"On removing the skull cap the dura was found markedly tense; an excess of cerebro-spinal fluid was present, distinctly turbid. About the pons and over the surface of the brain was a marked exudate, serous and sero-purulent, 1-3 mm. in thickness, through which the convolutions could be seen on the left. Over the right hemisphere, especially on the anterior superior surface, the exudate is 5-6 mm. in thickness, composed in places chiefly of recent hæmorrhage. On removing the dura this œdematous exudate is found to be a part of it, and numerous fine blood vessels may be seen arranged in a radial manner. In diameter, such circles measure 1½-2½ cm. About the base of the brain the exudate was more purulent in character. An incision into the ventricle is immediately followed by a gush of slightly turbid fluid. The sinuses are clear. No apparent infection is noted external to the dura. Middle ears appear normal."

Case 23.—No lobar pneumonia. Meningitis not benefited by Flexner's anti-meningococcic serum.

Med. No. 22,204. Female, æt. 7.

Sent to the hospital February 10, 1908, during an epidemic of cerebro-spinal meningitis, with a diagnosis of this disease.

*Family history and past history* unimportant.

*Present Illness.*—Six days before admission the patient came home from school complaining of pain in the back and the head and down the neck. These symptoms increased in severity during the night, and the next day she could not get out of bed and vomited everything taken into the stomach. The vomiting persisted during the next four days. On the third day of her illness she had two general convulsions and a third the following night, after which she became quite irrational. The patient had complained constantly of pain in the head, neck, and back, exaggerated by movement. Three days before admission the neck was held rigidly and the patient lay in bed with knees flexed.

*Physical Examination.*—The patient was admitted in a desperately sick condition. She was wholly irrational, lying with the knees drawn up, and moving the arms restlessly above the head. The neck was stiff and movements of the head caused pain, but there was no retraction of the head. An almost constant divergent strabismus was noted. The ears and mastoid region were apparently normal. The lungs and heart were clear. Both knee kicks were active. Kernig's sign was positive in both legs. Three lumbar punctures were performed. On the first day in the hospital 19 cc. of cloudy fluid, under 420 mm. of pressure, were removed. The fluid contained numerous polymorphonuclear leucocytes and was "simply swarming" with Gram-staining lanceolate diplococci. Cultures from this fluid subsequently yielded the *Diplococcus pneumoniæ* in pure growth. Spinal punctures, giving exactly similar results, were performed on three successive days, and at each of the three punctures 15 cc. of the Flexner antimeningitis serum was injected. The serum was absolutely without effect upon the cellular and bacterial content of the spinal fluid, and the fever, leucocytes, and symptoms remained unchanged. A culture from the blood, taken on the day of death, revealed the *Diplococcus pneumoniæ*. A few hours before death an area of consolidation was discovered in the low lobe of the left lung. During the three days the patient was under observation the leucocytes ranged from 11,000 to 14,000; the temperature between 104° F. and 107° F.; the pulse was constantly above 170, and the respirations rose steadily from 28 on admission to 96 at death, which occurred on the third day after admission to the hospital.

No autopsy permitted.

Case 24.—Lobar pneumonia (rt. and lt. upper) with abscesses; bilateral otitis media; meningitis.

Med. No. 23,572. Male, æt. 16 months. Colored.

Admitted January 10, 1909, complaining of pain and soreness in the left side, and died January 18, 1909.

The *family and past history* are without bearing on the present illness.

*Present Illness.*—The patient had always been quite well up to five days before admission, when he fell downstairs, striking his left side and shoulder. The next day the mother noticed that on picking the child up he cried apparently from pain. Since the fall, the mother said, the child had eaten practically nothing and had been very feverish. For four days prior to admission the patient had a paroxysmal cough, and the mother said the child's breathing had been very rapid.

*Physical Examination.*—On admission it was noted that the neck was slightly retracted, the legs were kept drawn up, and movement of the legs seemed to cause pain. There was no definite Kernig's sign. There were signs of pneumonic involvement of the left upper lobe. There was no discharge from ears.

The leucocytes numbered 21,000; the temperature was 104° F. to 102° F.; the pulse 160.

Four days after admission, which was the ninth day of disease, it was noted that the patient breathed with an expiratory grunt; there was slight internal strabismus of both eyes, and the neck was so stiff that the body could be lifted with the hand under the back of the head. The arms and legs were flexed and held rather rigidly. There was no arching of the back or retraction of the head and no Kernig's sign.

On the sixth day after admission a very definite redness was noticed about the left ear, and the patient complained when touched in the left mastoid region.

The leucocytes on this day numbered 47,900.

Lumbar puncture, performed on this day, revealed a clear, normal-looking fluid under pressure of 120 mm. of the fluid. On the following day a second lumbar puncture was performed and 10 cc. of cloudy, purulent fluid was obtained. Smears from the fluid showed characteristic encapsulated diplococci (*Diplococcus pneumoniæ*) and many pus cells.

The child died on January 18, 1909, the 17th day of the illness.

*Autopsy No. 3154.*—Anatomical diagnosis: "Lobar and lobular pneumonia with abscess formation (both upper lobes); acute fibrino-purulent pleuritis; acute splenic tumor; hyperplasia of lymphatic tissue of intestines; bilateral purulent otitis media; acute cerebro-spinal meningitis with hæmorrhage; cloudy swelling of viscera; hæmorrhage in adrenal."

*Head.*—"The lobes of both ears are swollen and œdematous. There is evidence of a purulent discharge."

*Brain.*—"The calvarium is removed with difficulty. The anterior fontanel is not closed, there being a diamond-shaped opening about 3 cm. in the long diameter. The dura and all the membranes of the brain are delicate. The pia-arachnoid is moist. The vessels are slightly congested. The meninges over the convexities of the cerebrum are slightly turbid, but no evidence of any purulent exudate is found anywhere. Over the pons medulla, cerebellar, and cerebral peduncles is a fresh, thin layer of blood, evidently a recent hæmorrhage into the pia-arachnoid. There is no evi-

dence of any exudate here. No ecchymoses are found anywhere. The brain was hardened in formalin. Section of it shows a slight congestion of the vessels, especially in the ependyma of the lateral ventricles. Otherwise it is normal.

Case 25.—Lobar pneumonia with abscess formation; very insidious development of meningitis; acute vegetative mitral and aortic endocarditis.

Med. No. 23,980. Female, æt. 50.

Was admitted to the hospital April 14, 1909, complaining of soreness of the chest and throat.

The *family and past history* were negative, except that the patient had been an immoderate drinker of whiskey and beer.

The *present illness* began 10 days before admission with a chill, pain in the left side, and cough. She had since been in bed with these symptoms and had gradually grown more lethargic.

On admission the *physical examination* revealed an emaciated old woman, breathing rapidly, and in a very dull mental condition. There were outspoken signs of lobar pneumonia of the left lower lobe.

The heart was not enlarged, but there was a systolic murmur following the first sound at the point of maximum impulse; no diastolic murmur audible.

The leucocytes numbered 15,000 upon admission. The temperature was 101° F.; pulse 100. The leucocytes fell during the following six days to as low as 6400, but on the day preceding the patient's death rose to 14,200, and upon this same day it was noted that the patient had grown much more stupid and that there was slight stiffness of the neck. No lumbar puncture was performed. The patient died April 22, eight days after admission to the hospital.

A blood culture, performed April 16, showed a pure growth of the *Diplococcus pneumoniæ*.

*Autopsy No. 3205.*—Anatomical diagnosis: "Lobar pneumonia with abscess formation; acute vegetative mitral and aortic endocarditis; acute pneumococcus meningitis; cloudy swelling of liver and kidneys; subacute and chronic pleurisy (left); chronic fibrous peritonitis, chiefly localized in the lesser peritoneal cavity; healed apical lesion (left); pulmonary emphysema; thrombosis of the left ovarian vein; chronic sclerotic endocarditis; colloid goitre; cholelithiasis."

*Brain.*—"The meninges are extremely œdematous. In the interstices of the pia-arachnoid over the convexity of the brain there are large accumulations of yellowish-gray, purulent material, which occurs for the most part along the course of the vessels. This exudate is most marked over the convexity of the brain, and occurs to a lesser extent over the lateral surfaces. The base shows a small amount of exudate, which occurs over the pons and along the optic chiasm and in the sylvian fissure."

*Bacteriological Note.*—"An extremely virulent pneumococcus was isolated."

# DELAYED RESOLUTION IN LOBAR PNEUMONIA.

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Among the conditions which can be counted on as sure to occur in a certain percentage of all cases of pneumonia is delayed resolution. We may define this as essentially a delay in the process of liquefaction, absorption and removal of the exudate. The question immediately arises as to what should be considered the ordinary period of resolution; what duration of time may be considered as normal and what as abnormal. Unquestionably in the ordinary run of cases there is considerable variation in the length of time required. It is probably safe to say that as a rule signs of consolidation are pretty well gone in a week or ten days after the crisis, certainly within two weeks. When one considers the conditions that may be present in any case of pneumonia, it is very evident that the laying down of a positive rule from the disappearance of all physical signs would be difficult; for example, there may be a considerable amount of exudate in the pleura which may give signs suggesting delayed resolution. In this study the occurrence of the complication in the medical clinic of the Johns Hopkins Hospital is considered. No cases are included about which there seemed to be any reasonable doubt as to the diagnosis. In deciding as to whether a case should be considered one of delayed resolution or not, it may be said that the minimum duration of signs in any case of this series was twenty-two days.

There are a number of points which demand special attention. Is the condition more likely to arise in debilitated persons? Does it occur more frequently after typical or atypical attacks? Is it more frequent in involvement of the apex, as is often stated? Have we any guide for the factors which determine it? It is surprising to find how little attention is given to the condition in many articles on pneumonia; some text-books make no mention of it whatever. Certain statements are apparently copied and repeated over and over again, without any basis, so far as the study of the cases in this series shows.

The condition as a rule is not a serious one beyond the delay and prolonged illness, as in the majority of cases the recovery is ultimately complete. To the physician, however, it brings a great deal of anxiety. There is always the possibility that some other complication may be present, as, for example, an empyema. Again the condition of the lung may suggest that perhaps the diagnosis has been wrong and the condition has really been a tuberculous and not an ordinary lobar pneumonia. The possibility that with the continuance of the condition there may be fibroid change is always a question to be considered.

Clinically there are several groups of cases:

1. In this the crisis occurs in the usual way or the termination may be by lysis and the temperature remains normal. The local features in the lung persist as before. The patient may be perfectly comfortable or may complain of a certain amount of pain and discomfort. There were 5 cases which may be put here.

2. In this the temperature drops gradually after the pneumonia, but does not reach normal, and there is a persistence of fever and of local signs in the lungs. The general symptoms may be marked, the patient showing prostration and more or less rapidity of the pulse. There were 20 cases regarded as belonging to this group.

3. There is a group in which the features are rather variable, the temperature may perhaps fall to normal and then recur with the signs in the lungs persisting.

*Incidence.*—Musser and Norris[1] found that delayed resolution occurred in 105 of 2548 collected cases (4.1 per cent). In the present series, among 805 cases (from May, 1889, to May, 1907), there were 30 of delayed resolution (3.7 per cent). There were 10 additional cases, the patient being admitted after the attack of pneumonia was over, so that 40 cases are available for study. In this series cases which might be regarded as slow resolution are not included and a persistence of signs for at least three weeks was regarded as essential. How much importance should be given to the existence of general symptoms, fever, cough, weakness, etc., as compared with the thoracic signs in deciding whether a given case shows delayed resolution or not, is difficult to decide. Practically it was found that most of the patients showed both local signs and general symptoms; even in the group with persistence of physical signs and no fever there was usually some rapidity of respiration.

[1] Osler's Modern Medicine, Vol. II, p. 590.

*Occurrence.*—In the study of the cases of empyema it was noted that the incidence varied greatly from year to year and that the maximum of its incidence coincided with that of pericarditis. However, there is no agreement in the years of greatest occurrence of delayed resolution. The years are as follows:

| | | | |
|---|---|---|---|
| 1891 | 1 | 1900 | 1 |
| 1894 | 1 | 1901 | 6 |
| 1895 | 1 | 1902 | 5 |
| 1896 | 1 | 1903 | 4 |
| 1897 | 3 | 1904 | 4 |
| 1898 | 1 | 1905 | 3 |
| 1899 | 1 | 1906 | 2 |
| | | 1907 | 3 |

There is a striking contrast between the numbers in the first and second halves of the eighteen-year period, namely 8 to 32. The same point is noted in the incidence of empyema, of which there were 5 cases in the first nine years and 24 in the second nine years. It would hardly be safe to draw the conclusion from these figures that both complications are on the increase. However, they were evidently more prevalent in this clinic from 1899 to 1907 than in the preceding nine years.

*Etiology.*—There are a number of factors to which importance is attached in the descriptions usually given. Thus, advanced age, alcoholism, cachexia, cardiac disease, venesection, involvement of the apex of the lung, etc., are all mentioned as contributing influences. It will be of interest to see how far these can be proved to have operated in this series.

*Age.*—The age incidence is as follows:

| Years. | Cases. |
|---|---|
| 11-20 | 4 |
| 21-30 | 18 |
| 31-40 | 8 |
| 41-50 | 9 |
| 51-60 | 1 |

That advanced age was a factor in these cases is definitely disproved by these figures. More than half the cases occurred between the ages of eleven and thirty, and only one was in the sixth decade, his age being fifty-three years. It is striking that the youngest patient was aged seventeen years; so the conclusion is that both the extremes of life are spared.

*Sex.*—There were 33 males and 7 females, the proportion in the whole pneumonia series being about 4 males to 1 female. This shows a higher relative proportion among males.

*Color.*—There were 17 whites and 23 colored patients, which shows a markedly higher relative incidence of the colored. The total admissions for pneumonia show a relatively high ratio of colored patients, the figures being about 3 white to 2 colored. In the total medical admissions the white and colored are in the ratio of about 5 to 1. Thus the colored patients comprise about 16 per cent of the total medical admissions, 40 per cent of the admissions for pneumonia and 57 per cent of the cases of delayed resolution. The increased ratio was evident both in the colored males and females. The colored patients comprised a relatively high percentage of the empyema cases, but this is not nearly so marked as in delayed resolution.

*Alcoholic History.*—Ten of the patients did not use alcohol at all; of the others 5 were slight users, 16 were moderate and 9 could be described as heavy drinkers. This must be regarded as showing rather a high occurrence of drinkers among the patients (75 per cent). The figure for the whole pneumonia series is about 65 per cent.

*Cachexia and Heart Disease.*—No patient of the series could be described as being cachectic and there was no instance of associated valvular disease. To decide how many of the patients had myocarditis would be difficult. This series does not support the view that these conditions favor delayed resolution. It has to be remembered that the majority of those with cachexia and probably many of those with cardiac disease—advanced at any rate—do not survive to have delayed resolution.

*Venesection.*—Only one patient of the series was bled. This was done twice on the sixth day for right heart enlargement, 300 cc. being removed each time.

*Lung Involvement in the Attack of Pneumonia.*—This is a point of considerable interest, especially in view of the importance so often assigned by writers to involvement of the apex. The figures here show a marked preponderance of involvement of the right side in the attack of pneumonia, the process being on the right side in 23, on the left in 12 and on both sides in 5 cases. One lobe was involved in 20 cases, two lobes in 11 and three or more in 9 cases. The number of times each lobe was involved in the pneumonic process was: upper right, 14;

middle right, 10; lower right, 23; upper left, 5; lower left, 16. This shows the much greater frequency with which a lower lobe was involved as compared with an upper in the patients who had delayed resolution, the totals for the lower lobe being 37 and for the upper lobe 19. When only a single lobe was involved the figures are: upper right, 5; lower right, 6; upper left, 1; lower left, 8. The whole right side and the whole left side were each involved in 3 cases, and the lower lobes in 3 cases. In the remainder there were various combinations of lobes. These figures show the more frequent involvement of the right side as compared with the left (23 to 12, when the process was on one side only, and 45 to 21, when the total number of lobes is counted). The greater frequency of involvement of the lower lobes is also evident, the figures when only one lobe was involved being 14 lower to 6 upper; and if the total number of times any lobe was involved is counted, the totals are 37 for the lower and 19 for the upper (middle right lobe, 10).

*Lobe Involved in the Delayed Resolution.*—The study of this point is of interest especially in connection with the statement so often made that the apex is frequently involved. The figures are as follows: lower right lobe in 19 cases (part of the middle lobe being also involved in one); lower left in 8; upper right in 6; upper left in 3; both lower lobes in 2; and the upper and lower right lobes in 2 cases. This shows about the same relative preponderance of the right side as was found in the involvement in the attack of pneumonia. The delayed resolution was on the right side in 27 cases; on the left side in 11; and on both sides in 2 cases. In 36 cases one lobe only was involved; in 2 the upper and lower right lobes; and in 2 both lower lobes were involved. In the cases in which one lobe was involved, 25 were on the right side and 11 on the left side. Taking the total lobes involved the figures are 31 for the right side and 13 for the left. As regards the upper and lower lobes the figures are 27 for the lower lobes and 9 for the upper, when one lobe only was involved.

There are two points which attract attention, the frequency with which the process occurred on the right side, and the rarity with which more than one lobe was affected. Why should one lobe clear and another not? One lobe only was involved in just half of the cases in the attack of pneumonia, but in 36 of 40 with delayed resolution. That is, of 20 cases in which more than one lobe was involved in the pneumonia, in 16 the delayed resolution occurred in one lobe only. Again, why

should the lower right lobe predominate so markedly, being nearly equal to all the other lobes put together? It is very evident that this series gives no support to the view that delayed resolution is especially common in apical pneumonia, quite the contrary.

A comparison of the figures of the extent of lung involvement in these patients shows that there was some agreement, except in the case of the middle right lobe.

| Lobe. | Involved in pneumonia. | Showed delayed resolution. |
|---|---|---|
| Upper right | 14 | 8 |
| Middle right | 10 | 1 |
| Lower right | 23 | 23 |
| Upper left | 5 | 3 |
| Lower left | 16 | 10 |

In taking the figures of involvement for the whole pneumonia series we find that the relative ratio of the right side to the left, when the process was only in one lung, is about as 2.1 to 1 (in delayed resolution about 2.5 to 1). Both sides were involved in 20 per cent of all cases, but only in 5 per cent of the cases of delayed resolution. There was involvement of only one lobe in 50 per cent of all cases (in 90 per cent of the delayed resolution), and 61 per cent of these were on the right side (70 per cent of the delayed resolution). Taking the total number of times a lobe was involved, either alone or with others, in the whole pneumonia series and comparing this with the number of times delayed resolution occurred in each lobe, the figures are: upper right lobe, 1 in 27.5; lower right, 1 in 16.2; upper left, 1 in 31.6; lower left, 1 in 27.3. Only one instance of delayed resolution occurred in the right middle lobe and this only involved a part of it. These figures bring out the much greater relative frequency of the process in the lower right lobe. The figures for the upper right lobe and for the left side are much the same, delayed resolution occurring approximately about once in thirty times, but in the lower right lobe it was nearly twice in thirty times.

The figures of this series show that the lower right lobe is involved in delayed resolution relatively more frequently than any other. The larger number of instances of delayed resolution on the right side as compared with the left corresponds to the more frequent occurrence of pneumonia on the right side. But the question arises as to the relatively much greater frequency of delayed resolution in the lower right

lobe. The matter of the circulation can hardly be regarded as having any influence. Why should there be any difference in ferment action in the two sides? For example one patient had involvement of both lower lobes. The termination was by lysis on the eighth day. By the seventeenth day the left side had cleared entirely, but the right showed no sign of resolution. The anatomical condition and the relation to the liver may be suggested as an explanation. It would be of interest to follow a series of patients with pneumonia to determine whether the normal expansion returns more quickly after involvement of the lower left than of the lower right lobe. In healthy young women there is often a good deal of difference in the expansion of the lower right and left thorax, the right showing less movement. The breath sounds over the lower right lobe in these persons also show some change, being less well heard than over the left. These differences are most evident immediately after removal of the clothing; and this (corsets especially) may have had some influence. Both the difference in expansion and in the breath sounds became less marked after some deep breaths were taken. That diminished respiratory movement on the lower right side can account for the greater frequency of delayed resolution in the lower right lobe may be suggested, but cannot be regarded as proved.

As regards the whole question of etiology, some of the factors usually considered as important cannot be so regarded in view of the study of this series. Its special frequency in apical involvement is not supported, quite the contrary. Any special frequency is associated with pneumonia in the lower right lobe. Alcoholism can hardly be said to be of great importance, although the percentage of users of alcohol is slightly higher among the patients with delayed resolution than among the whole series. Cachexia, advanced life and cardiac disease did not figure. Altogether this series shows as factors, the color of the patient and involvement of the lower lobe.

The essential etiological factor must be associated with some interference with the usual process which occurs in the removal of an exudate. This in the case of a pneumonic exudate must be by one of three ways: (1) absorption, (2) organization and (3) removal by the bronchi. The last of these must be of very slight importance and in many cases probably does not enter into the process at all. Flexner[1] has discussed the point and points out that in the process of absorption

[1] University of Pennsylvania Medical Bulletin, 1903, XVI, p. 185.

disintegration and solution of the cells take place, with the formation of an emulsion which can be absorbed. In the process of organization new vessels invade the exudate and by supplying a fresh set of leucocytes the material is removed. The leucocyte is apparently the essential agent in the process and it does not seem to matter whether the leucocytes are living or dead. Flexner points out the difference in resolution in a caseous and croupous pneumonia as probably depending in large part on the difference in the number of leucocytes present. The importance of this is seen in the difference in the process of autolysis in the stages of red and gray hepatization, it being very slight in the former.

Flexner sums up the question by saying that he is inclined to view unresolved pneumonia as an acute lobar pneumonia in which the inflammatory exudate, either because of some disproportion between the leucocytes and other constituents or other cause as yet unknown, failing to autolyze, cannot be absorbed and hence undergoes organization.

*Pathology.*—The findings must depend largely on the time of death. Thus if a patient dies soon after the termination of the pneumonia from a complication, such as endocarditis, the condition of the lung will not differ materially from that found during the pneumonic attack. The condition, if it persists sufficiently long, is not to be distinguished from that termed sometimes chronic pneumonia, although the term cannot be regarded as a good one. The accounts of the autopsies in the two fatal cases of this series illustrate some of the points.

In one (No. 3927) the patient was admitted with the complaint of weakness, two weeks after the onset of the attack of pneumonia. There was diminished expansion on the right side with tympany in front down to the fourth rib, below which there was dulness which extended through the axilla and lower back. Vocal fremitus was present throughout. Over the area of dulness there was tubular breathing with a few crackling râles in the back. The leucocytes were 16,000. At the end of a week the dulness was higher in the back, tubular breathing was still present over the dull area and coarse bubbling râles were heard in the back. The temperature varied from normal to 100° F., after being subnormal. The pulse varied from 100 to 120. The patient died on the twenty-fifth day.

At autopsy the lower right lobe and part of the middle lobe were found to be solid. The pleura was adherent over the greater part of the lung, and between the lower part of the lung and the diaphragm there was a small empyema. The upper lobe showed hyperæmia, but no consolidation.

The upper left lobe was emphysematous; the lower left lobe showed some small areas of consolidation. The pleura was everywhere adherent. There

was a suppurative pericarditis. Sections of the lower right lobe showed some empty alveoli, but the majority were full of cells. The fibrin present was small in amount. Everywhere there was fresh interstitial connective tissue, the cells having long spindle-shaped nuclei. In places this seemed to be continuous with the interalveolar connective tissue. The pleural adhesions were organizing.

In this case, at the end of twenty-five days from the onset of the attack of pneumonia, there was definite evidence of organic change in the lung. So far as clinical observations may be regarded as a guide, delayed resolution may persist longer than this and complete recovery result.

In another case (No. 18,606) the patient was admitted on the fifth day with a moderately severe attack. The temperature fell by lysis from the eighth to the eleventh day and was then normal until the seventeenth day, after which it was irregularly elevated. On the twentieth day there was a shaking chill and the temperature rose to 105° F. With this there was no change in the signs which had persisted in the lower right lobe. On the twenty-second day there was dulness and increased vocal fremitus over the lower right back. The breath sounds were distant and accompanied by râles. In addition there was a friction rub. There were definite signs of endocarditis, which was probably the cause of the chill and high fever. By the twenty-fifth day the patient had lost much weight. The signs over the lower right lobe were clearing. Death occurred on the fifty-seventh day.

At autopsy the right pleural cavity was almost obliterated by fresh vascular œdematous adhesions. The lower lobe contained some air, but was firmer than normal and there was a definite increase in the interstitial tissue. Sections showed a small amount of inflammatory exudate in the alveoli. There was definite increase in the fibrous tissue and granulation tissue was growing out in the alveolar exudate. The pleura showed marked increase in tissue. The bronchial glands were swollen and showed increase of connective tissue.

The most striking feature is the new formation of connective tissue. This may begin in the fibrinous contents of the alveoli or may proceed from proliferation of the connective tissue in the blood-vessels in the tissue of the alveolar wall. In some cases the connective-tissue cells are seen projecting like plugs into the alveoli. They contain newly-formed vessels. In other cases the connective tissue communicates with the trabecular framework. In all cases the tendency is towards contraction and obliteration of the alveoli, the exudate in them being often dense and hyaline and poor in cells.

*Symptoms. Onset.*—Naturally there cannot be said to be any definite time of onset as regards the symptoms, for the process, in the

majority of patients, is really a continuation of that present during the pneumonia. In a few instances there was a period after the crisis or lysis during which the patient felt fairly well, to complain later of other symptoms. The most common complaints were of some respiratory distress, thoracic pain, cough and weakness. When the patients were under observation during the attack of pneumonia, the complaints due to the delayed resolution were not specially in evidence. They were brought out in patients who had the attack of pneumonia outside the hospital, had recovered, as they thought, and then came in on account of symptoms which they regarded as distinct from those of pneumonia. The complaint of weakness was quite common, several of the patients having gone back to work, but having to desist on account of lack of strength. It is of interest to note that in some patients there was a period of gain in strength after the termination of the pneumonia, which was followed later by a loss of strength. In regard to the complaint of thoracic pain it may be noted that this sometimes appeared in the course of the delayed resolution. In some cases it was associated with the presence of a friction rub.

The general features are perhaps best illustrated by an account of a case:

The patient was admitted on the fifth day of the disease, with involvement of the upper and lower right lobes. The temperature fell by lysis on the ninth and tenth days, reaching 99° F. on the tenth day, but afterwards rising and remaining more or less elevated until the thirty-first day. After this it was rather irregular, touching normal each day until the fifty-fourth day, after which it remained normal. With the lysis the patient's general condition improved, but there was still some discomfort and slight dyspnœa. The signs in the lung persisted; thus on the eighteenth day there was marked restriction of motion on the right side, dulness and rather distant breath sounds over the right lower lobe. From this to the thirty-eighth day the patient's general condition was slowly improving, but the signs in the chest remained about the same. On the thirty-eighth day a friction rub became audible over the right lower lobe. Up to this time there had been distinct tubular breathing. From the thirty-eighth to the forty-fifth day the most marked change in the signs was that the tubular breathing was becoming less marked and more distant. By the fifty-sixth day it was almost entirely gone and many coarse, moist râles were heard. The patient was not discharged until the eighty-first day, when the signs in the lung had practically cleared. He had gained weight and was discharged in good general condition. The leucocytes during the pneumonia varied from 40,000 to 50,000. From the tenth to the twenty-fifth day they were between

30,000 and 17,000 and then after a time they dropped to about 12,000; rose again on the fortieth day to 25,000 and after this came down to about normal. The pulse during the pneumonia was between 100 and 120, after this came down gradually to about normal. The respirations showed the same decline.

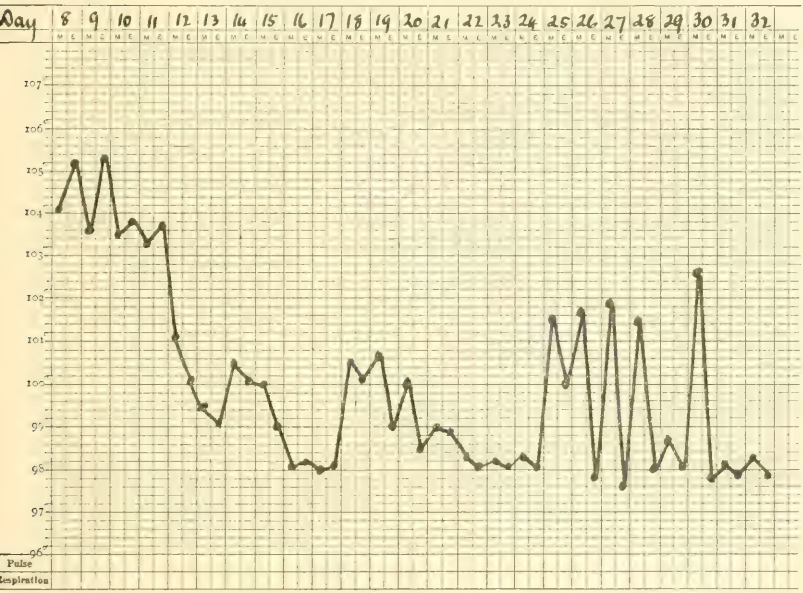


FIG. 1.—Admission on the eighth day of the pneumonia. Crisis on twelfth day. Irregular fever afterwards. Resolution in sixth week.

In another form of case the chief difference is that the temperature falls to normal either by crisis or lysis and remains there, but the signs in the lungs persist. The patient may be gaining in strength and feeling fairly well despite this. Such was the case in one patient in whom the signs did not clear until the fiftieth day, although there was a constant gain in weight and strength. The general condition

varies a great deal; some patients being quite comfortable and fairly well, others complaining of weakness and cough and making very little progress in general improvement.

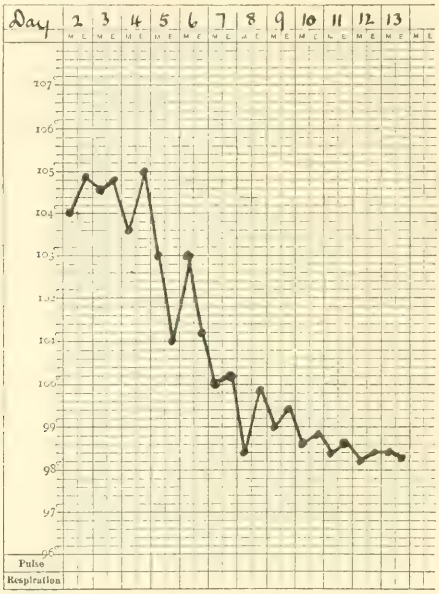


FIG. 2.—Admission on the second day of the attack of pneumonia. Temperature practically normal on the ninth day. Resolution in the fourth week.

*Physical Signs.*—Naturally these vary with the stage of clearing and those present during the early part of the condition will be described first. The study of the physical signs is especially important as regards diagnosis. The condition, while in itself usually not very serious for the patient—there are some exceptions—is decidedly so for the peace of mind of the physician. He fears that perhaps he is overlooking an empyema or that the process may be tuberculous. To the man who has

confidently talked of a crisis on the seventh day, delayed resolution emphasizes the importance of caution in joining himself to the ranks of the prophets. Then the question of treatment is an important one and much may depend on an early diagnosis.

*Inspection.*—This usually shows diminished expansion on the affected side, which persists from the pneumonia. The condition of the interspaces does not, as a rule, show any special features.

*Palpation.*—The most important point is the observation of the vocal fremitus. As was noted in discussing empyema, the findings in it are often very puzzling and apparently against the rule. The same is true in delayed resolution. Theoretically we should expect that tactile fremitus would be increased over the affected area. The results are as follows in 32 cases in which the notes are positive: in 8 the vocal fremitus was about normal; in 13 it was increased; in 10 it was definitely diminished, in one of these being almost absent; and in one it was absent. When one searches for an explanation of the decrease, there are several factors. One of these is that several of these patients coughed up casts of the bronchi; not large moulds as one sees in fibrinous bronchitis, but still fairly large and evidently not from the small bronchi. Unfortunately it was not noted whether the fremitus was more marked after this occurred. In several other cases there was a well-marked friction rub present at the time and there may have been enough exudate to interfere with the transmission of the fremitus. Another explanation may be suggested in the anatomical conditions present. In one case coming to autopsy it was found that a certain number of the alveoli were free of exudate, while others contained it; at the same time there was some increase of connective tissue. It is possible that this combination of conditions might result in a decreased conveyance of vibrations. However, probably the most common cause of decreased vocal fremitus lies in the presence of exudate in the pleura. When we remember how commonly at autopsy on patients dead of pneumonia a thick layer of exudate is found, it is not difficult to understand how such a condition would lessen the vocal fremitus.

*Percussion.*—This showed dulness over the affected lobe in all cases, but the degree varied greatly from moderate impairment to flatness. With this there was also increased resistance. It would be impossible to speak with certainty as to any special quality of the percussion note being characteristic of delayed resolution, for while absolute flatness

was noted in some instances, yet in many the note had not the wooden quality so often obtained over fluid. As regards diagnosis in doubtful cases no importance can be attached to any special quality in the note. The point of interest is the occurrence of tympany. This, of course, is not uncommon in pneumonia at the beginning of consolidation and during resolution as well. Tympany was found in part of the lobe in which resolution was delayed in 7 cases. In 5 cases tympany was marked in another lobe, which had been consolidated, and it may be noted here that when delayed resolution was marked in the lower lobe, for example, the other lobe which was consolidated often seemed to clear more slowly than normal, but not so slowly that it could be regarded as delayed resolution. In one case there was tympany over the adjoining part of the next lobe, which had not been affected in the pneumonia. In one case, in which the resolution was delayed in the lower lobe, there was an area of tympany so marked over a small area below the angle of the scapula that had the patient come under observation then for the first time, a cavity would have been suspected. This occurrence of tympany does not greatly differ from that found in pneumonia itself and probably the explanation is the same in both cases.

As regards the diagnosis of delayed resolution, the results of percussion offer nothing very distinctive. It is a characteristic sign of the condition, but does not offer any aid in distinguishing it from other conditions, except perhaps in the fact that the note over the lung, which shows delayed resolution, is not as dull as that often found over fluid.

*Auscultation.*—The results of this are very varied and it is quite impossible to make a definite statement as to any one condition being the rule. This applies both to the findings during the period of delayed resolution and during the period when the lung is clearing.

First, taking up the signs on auscultation during the period of delayed resolution, it is surprising to find how variable they are. Feeble tubular breathing, but without any râles, was the finding in 6 cases, and feeble tubular breathing, with râles, which were usually fine and crackling, but coarse and moist in some, in 11 cases. Tubular breathing of moderate intensity was heard in 6 cases; in 3 accompanied by râles. There was intense tubular breathing, without râles in 3 cases; with moist râles in 2 cases; and with crackling râles in 1 case. In 9 cases there was no tubular breathing. In 3 of these the sounds were distant, feeble and of vesicular quality, without any accompanying râles;

in 4 cases, with the same breath sounds, there were râles, these being fine crackling in 2, and coarse in 2. In 2 there were harsh breath sounds, without any tubular quality. When these observations were made there were no signs of clearing, unless the disappearance of tubular breathing be regarded as such. The voice sounds were usually conveyed more loudly than normal and this did not bear any relationship to the character of the breath sounds, for in some cases, with feeble breath sounds or very feeble tubular breathing, the voice sounds were transmitted more loudly than normal.

The signs during the process of clearing were, if anything, more diverse. The most common change was that the breath sounds became less tubular and râles appeared, as was found in 11 cases. In 5 cases the breath sounds became less tubular, but there were no râles in 2 at any time, while in 3 a few appearel later on and were never marked. In 2 cases the tubular breathing became gradually less marked and the râles disappeared. In 9 cases the breath sounds became enfeebled during the clearing, in 5 of these no râles being heard. In one other there were a few fine râles, with the same change in the breath sounds. In 3 the breath sounds became harsh, but not tubular; in 2 they were accompanied by crackling râles, and in 1 other there were no râles. In 1 case, in which the breath sounds had been very feeble but not tubular, they gradually became louder, but without any râles. In one case the only change was that the râles became louder and more numerous. A pleural friction rub appeared in some cases during the clearing.

Two cases may be quoted which showed marked variations:

(No. 15,395.) The patient was admitted with involvement of the lower right lobe. The course was prolonged and apparently there was gradual extension, consolidation in the lower left lobe being found on the tenth day. On the eleventh day the general condition was better. The lower right lobe, the one first involved, began to show signs of clearing. The temperature dropped somewhat from the twelfth to the fourteenth day and again after the sixteenth day. On the sixteenth day there was dulness over both lower lobes and tubular breathing on both sides, which was much more marked on the left. On the nineteenth day the dulness was much more marked over the lower left lobe than on the other side. The tubular breathing could be heard on both sides. On the twenty-second day the condition was much the same except that vocal fremitus was almost absent over the lower left lobe. On the twenty-seventh day the temperature rose and continued elevated to the thirty-fifth day. By this time the left side had

cleared fairly well; the resonance was almost normal, tubular breathing had disappeared and the breath sounds were well heard, accompanied by many coarse râles. There was still dulness over the lower right lobe, vocal fremitus was well marked and the breath sounds were still distant, with a slight tubular quality and accompanied by many coarse crackling râles. In this case there was delayed resolution in both lower lobes, the right showing some signs of clearing early, but the left ultimately clearing up much sooner than the right.

In another case (No. 17,076) the patient had involvement of both upper and lower left lobes. The temperature fell slowly from the eighth to the twelfth day. On the sixteenth day the note on percussion over the lower lobe was clearing, the breath sounds were very feeble, there was marked dulness over the upper lobe with distinct tubular breathing. On the twenty-second day there was slight fever, dulness over the upper left front, with increased vocal fremitus, and diminished breath sounds which were not tubular. In the back there was dulness and tubular breathing. Over the lower lobe there was slight dulness, but the breath sounds were almost normal. On the forty-sixth day there was quite marked change in the shape of the left side with drooping of the left shoulder, asymmetry of the chest and very little expansion of the upper left thorax. There was marked dulness from the apex to the fifth rib in front, with tubular breathing above the clavicle and practically nothing at all heard below it until about the fifth rib, when feeble breath sounds became audible. There was dulness in the upper left back, with distant tubular breathing. Over the lower left back the note was fairly clear, but the breath sounds were very distant. The temperature fell to normal on the fiftieth day; the patient was discharged on the sixty-fifth day with the left side clear on percussion, vocal fremitus being slightly increased and the breath sounds hardly as loud as on the right side. This is an example of the variability that there may be in the signs.

*Friction Rub.*—This was heard in several cases after the usual features of the pneumonia had disappeared. Thus in 1 case a friction rub was heard on the seventeenth and in another on the twenty-eighth day; otherwise there were no special changes in the physical signs. This late appearance of a friction rub may be due to an extension of the process to the surface of the lung or possibly to absorption of exudate which had been present. In both the autopsies in this series fresh pleural adhesions were found.

*Fever.*—The termination of the attack of pneumonia was usually by lysis, crisis occurring in 4 cases and a pseudo-crisis in 1 case. In 2 cases there was neither crisis nor lysis, the fever running on continuously. In the majority of cases the temperature fell, but persisted, as occurred in 20 cases. In 5 cases it fell to normal and remained

there; in 3 others it fell to normal, but rose again after a few days. The degree of fever varied greatly. In the largest number, 16, it varied from 99° to 101° F.; in 5 it varied from 99° to 102° F.; in 5 from 99° to 103° F.; in 7 from normal to 100° F.; and in 1 from normal to 103° F. There was much variation in the duration of the fever; of

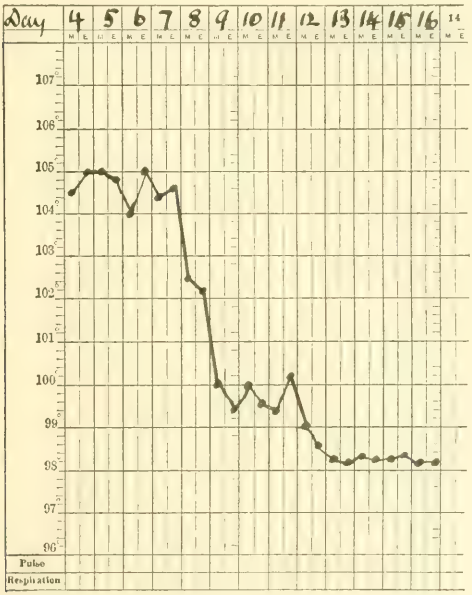


FIG. 3.—Admission on the fourth day of the attack of pneumonia. Normal temperature on the twelfth day. No fever subsequently. Resolution in the fifth week.

those cases in which it persisted the earliest termination was on the fourteenth day; the longest was to the fifty-fourth day. The fever lasted to the third week in 7 cases; fourth week in 4 cases; fifth week in 7 cases; sixth week in 4 cases; seventh week in 2 cases; and eighth week in 2 cases.

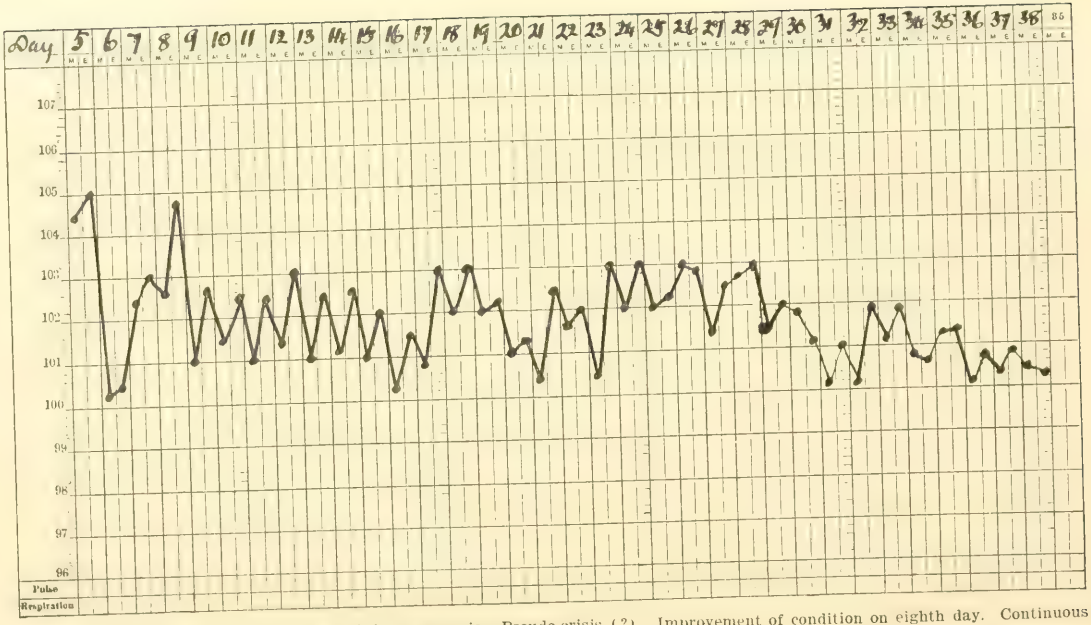


FIG. 4.—Admission on the fifth day of the pneumonia. Pseudo crisis (?). Improvement of condition on eighth day. Continuous fever until the fifty-second day. Resolution in eighth week.

One of the points which is stated in regard to the character of the attack of pneumonia is that this is often atypical. How much the termination by lysis is evidence of this may be questioned. Certainly in this series the number terminating by crisis is small, only 4. If the occurrence of delayed resolution is determined before the termination of the attack, it is easy to understand why crisis should be rare. But again we are met with the difficulty of determining why it occurs. The degree of toxæmia in pneumonia does not bear any relationship to the amount of lung involvement, and it is hardly justifiable to consider that a partial clearing of the consolidation may determine a partial decrease in the features such as fever. In some cases, although the consolidation persists and resolution is delayed, the general features, such as fever and toxæmia, are entirely absent. Yet these are decidedly in the minority.

*Pulse.*—This showed great variation, but it is noted that marked rapidity was not of frequent occurrence; in only 1 case was a persistent rate over 120 found. In 5 the rate was practically normal, not being over 80. In 3 the rate was not over 90. In 12 the rate varied between 80 and 100. In 10 from 80 to 120. In 1 case from 120 to 136. *Bradycardia* occurred in 3 cases; in 1 a rate of 56 to 60 persisted; in 2 others a rate of 50 to 60 persisted for a time, following a rate of 80 to 100. As a rule, with the process of clearing the rate gradually fell to normal.

*Respiration.*—This varied as the pulse, but the patients with rapid pulse rate did not necessarily have an increased respiration rate. The rate varied from 20 to 24 in 5 cases; from 24 to 26 in 3 cases; from 24 to 28 in 8 cases; from 28 to 32 in 2 cases; from 28 to 44 in 1 case; from 24 to 36 in 4 cases; and over 30 in 7 cases. A rate over 40 was present for some time in 5 cases. In 1 patient the respiration rate, which during the pneumonia had varied from 48 to 60, remained between 28 and 36 until the lung had cleared, and for some days after all signs of delayed resolution had gone varied from 24 to 28. There was no other condition present to account for the increased rate.

*Leucocytes.*—These showed very great variations. As a rule leucocytosis was present, which showed changes from day to day. Generally this was in the direction of a gradual decrease, but this was not invariable; thus in one patient, when the temperature fell almost to normal on the fifteenth day, the leucocytes were 15,000. The signs in the lung persisted and by the twentieth day the leucocytes were

12,000. After this the general condition improved rapidly and the lung cleared fast, but on the twenty-seventh day the leucocytes were 27,000, without any other explanation being found.

In 7 cases the leucocytes were practically normal, not being over 9000; in 3 others they were not above 12,000. The others showed all degrees, the highest figure being 50,000. In 5 cases the leucocytes were between 10,000 and 15,000; in 7 cases not over 20,000, and usually between 10,000 and 20,000; in 9 they reached between 20,000 and 30,000; in 5 they were over 30,000. It was not possible to associate their number with the course of resolution, the persistence of signs or the degree of temperature. In several cases there was a marked leucocytosis, with a normal temperature. Thus in 1 case there were 50,000 on the thirteenth day; the temperature reached normal on the fifteenth day and on the sixteenth day the leucocytes were 31,000, dropping gradually to 15,000 on the twentieth day; during this time the signs in the lungs were clearing. There were often marked variations. Thus in 1 case during the pneumonia the count was not greatly increased, varying from 5000 to 12,000, but afterwards they ran to 27,000 and then dropped to about 15,000 for some time. In another they were about 25,000 during the pneumonia; by the eighteenth day they were 15,000; and on the twentieth day 12,000. The lung cleared rapidly from the twentieth to the thirtieth day, but on the twenty-seventh day the leucocytes were 27,000.

In general it may be said that leucocytosis is the rule in the majority of cases, but it is not so invariable that its absence or presence could be used as a diagnostic point. The cases with empyema showed leucocytosis much more constantly, so that the absence of leucocytosis speaks against empyema and in favor of delayed resolution, when the diagnosis lies between the two.

*Sputum.*—The character of this showed considerable variation. In the majority it was muco-purulent and tenacious. The latter characteristic often persisted for some time; in one patient the sputum was still quite tenacious in the seventh week. In several cases it was watery and occasionally purulent. Small amounts of blood were common for some time after the pneumonia, and in one case persisted till the fourth week. In one the sputum was very foul, and this persisted until recovery. Prune-juice sputum was noted in one case. A few patients had very frothy sputum. Taken altogether no description of the sputum can be given which could apply generally.

*Cast of a Bronchus.*—One patient brought up a large fibrinous cast of a bronchus in the fourth week. This is exceptional and is usually described as being an early phenomenon and corresponding to the stage of hepatization. Only once did Biermer find bronchial casts and symptoms of hepatization three weeks after the observed beginning. Two other patients of this series brought up small casts.

*Excretion of Chlorides.*—This in common with most of the findings showed much variation and no constant results were found. Thus some cases showed an output much below normal throughout the whole course and even when the lung had practically cleared. In others there was a great increase in the amount about the time that resolution proceeded most rapidly. Curious alterations in the amounts were seen from time to time, often varying from day to day. As a rule it may be said that the excretion tended to increase rapidly with the resolution, but in some cases it was only after a period of some weeks that they reached the normal output.

*Unusual Features. Collapse.*—This was seen in one patient who had a fairly severe attack of pneumonia, which terminated by lysis. Fever continued after this until the sixteenth day, when the temperature fell to normal, remaining there until the twenty-second day, after which it rose again. The signs in the lower right lobe persisted unchanged. On the twenty-fifth day the patient was quite comfortable and his general condition was good; the signs in the lung were as before. The leucocytes in the morning were 10,000. In the evening he had a sudden attack of nausea and then suddenly collapsed. With this the respirations increased in rate and were shallow. The pulse rose to 140 and became very feeble. For some hours it seemed that the patient was going to die, but he gradually improved and the next day seemed as well as before. At this time, and for some days afterwards, he brought up large amounts of frothy sputum. There was no change in the signs in the lung.

*Chills.*—A definite shaking chill occurred in one case, but as there was endocarditis in addition to delayed resolution, the cardiac complication was probably the cause. *Sweating* also was unusual and a heavy sweat occurred in 1 case only. This was on the seventeenth day, when there was irregular fever, marked signs in the lung and prune-juice sputum.

*Psychosis.*—There was only one instance of this in the series. The patient was admitted on the eighth day of a severe attack. He was

wildly delirious on the ninth day and was difficult to restrain; the high fever continued. On the tenth day his mental condition was somewhat improved and he recognized his relations. By the twelfth day the mental condition had changed from noisy violent delirium to a dull apathetic state in which he refused to answer any questions. On the thirteenth day he had a remarkable facial expression. He lay staring at the ceiling with the eyes kept motionless and very rarely showing any winking. He resisted any movement. There was no stiffness of the neck or Kernig's sign, but in view of the symptoms, lumbar puncture was done. A small amount of fluid was obtained, cultures from which were negative. On the fourteenth day he lay perfectly quiet, took no notice of what was going on about him, kept the eyes fixed and winked very rarely. There was a moderate grade of catalepsy and the arms remained in whatever position they were placed. About this time the temperature fell gradually, but the signs in the lung persisted. By the twentieth day the general condition was improved, but the mental state was much the same. The patient refused to take any nourishment and was fed with difficulty. He would not answer questions and did not take any notice of what was going on about him. By the twenty-fifth day the signs in the lung were diminishing, but the mental condition changed suddenly from the dull apathetic state to a violent condition. He became very antagonistic and opposed everything that was done for him. He refused to eat, saying that attempts were being made to poison him. He had to be fed by stomach tube and rectum. He said the nurses and attendants were tormenting him and trying to injure him. At times he described men who came and stood beside his bed, some of whom he called by name. He also described men who lighted fires beside his bed, but this did not in any way alarm him. During the greater part of the time he lay perfectly quiet and did not move, but he had periods in which he attacked the attendants and indulged in violent tirades of abuse. After these he was very quiet for a time and stated that he was in heaven. This did not seem to afford him any more gratification than the lighting of the fires about him had caused him alarm. By the thirtieth day the signs in the lung had cleared markedly. He began to eat food, but refused to drink any liquid while anyone was in the room with him. When left alone he drank liquids freely. At this time he passed his urine and fæces in the bed and resented the attempts to keep him clean. On the thirty-fourth day he suddenly turned against

his relations. At this time he remembered his name, but had no recollection of his illness, where he lived or where he had worked. There was still some slight fever. By the forty-third day the lung had cleared, but the mental condition was much the same. He was removed from the hospital by his family and his course could not be followed, but it was found some time later that he recovered perfectly. In this case there was delirium of the ordinary form during the attack of pneumonia. The psychosis did not appear until after the attack was over and persisted longer than the delayed resolution, although we were not able to learn the exact duration. It is impossible to say that it was specially due to the delayed resolution, as it might have occurred from the pneumonia alone.

*Signs on Clearing.*—It is not easy to say in many cases with certainty what was the first sign of clearing. As a rule some change in the percussion note was most evident. In the majority this was that the note became less dull, but in some cases a quality of tympany became evident. The clearing was sometimes rapid; thus in 1 case there was practically entire disappearance of dulness in five days. In the cases in which fever persisted there were usually signs of clearing before the temperature dropped to normal. As to the first changes in the signs on auscultation, when these could be determined, a common alteration was a diminution in the intensity of the tubular breathing. This occurred in 15 cases, in a few of which it was accompanied by the appearance of râles, some being moist and some dry and crepitant. In 16 cases the most marked change was that the breath sounds became feebler and distant. With this the tubular quality became less marked, but the most pronounced change was the feeble distant character of the sounds. This is certainly a curious finding and one rather difficult of explanation. It may be that in some cases the bronchi are plugged, which is supported by some patients bringing up casts of the bronchi. As the clearing advanced the breath sounds gradually returned to normal, but in several patients they were still more feeble than normal, after all other signs had cleared.

*Duration of Resolution.*—It is difficult to determine this with certainty, but in some cases it could be estimated with fair exactness. From the time when signs of clearing were first evident until the lung was practically normal, in 5 cases the interval was about ten days; in 8 cases about fifteen days; in 5 cases about twenty days; in 7 cases about twenty-five days; in 5 cases about thirty days; and in 2 cases

about fifty days. In the others the period was uncertain. No instance of very rapid clearing was seen (except 1 of five days, already noted), and the average time after resolution began was much longer than that seen in the usual resolution after the attack of pneumonia. Even here, however, it must be rare to see cases, such as Aufrecht mentions, in which complete clearing occurred in from twenty-four to forty-eight hours.

*Diagnosis.*—There is no necessity for emphasizing the importance of the early recognition of delayed resolution. We are all familiar with the worry which the condition gives, both to the patient and to the physician. The latter has the uncertainty as to whether he may not be overlooking an empyema, or be dealing with a tuberculous pneumonia. Then again, if it be delayed resolution the matter of proper treatment must be considered; if by this we can hasten the resolution, it is important to do so, as by this we may prevent the development of permanent change. On the other hand, it is important not to use the X-rays in such a condition as tuberculous pneumonia. The study of the physical signs in empyema and delayed resolution shows how very uncertain these are and how hopeless it is to trust to the presence or absence of any one sign in making the diagnosis.

None of the general features can be considered as at all typical of delayed resolution. Any of them may occur with a tuberculous pneumonia or with empyema and the exact termination of the condition must often be a matter of the exclusion of other possibilities. The important conditions which have to be excluded are as follows: (a) empyema; (b) tuberculous pneumonia; (c) the gradual extension of the consolidation; and (d) chronic pneumonia. In some cases possibly new growth or syphilis of the lung may give difficulty.

(a) *Empyema.*—The difficulties in this may be illustrated by the account of one of the cases in this series:

The patient was admitted on the fourth day of the disease with involvement of the lower right lobe. The attack was severe, with jaundice and marked toxæmia. The temperature fell somewhat on the seventh and eighth days, but did not reach normal, and from the eighth to the thirteenth day varied from 100° to 101° F. On the eighth day there was dulness in the right axilla and flatness in the lower right back and an almost complete suppression of breath sounds in the lower axilla, the breath sounds in the back having a tubular quality, but being typically tubular over only a very small area in the lower interscapular region. A few crepitant râles were heard. On the eleventh day the patient's general condition was better

and he was more comfortable. Dulness persisted over the lower lobe, vocal fremitus was almost entirely absent as well as the breath sounds and voice sounds. No friction rub was heard and no movable dulness was made out. These signs naturally suggested effusion and accordingly a needle was inserted, which evidently went into the lung, and only a few drops of bloody fluid were obtained. By the fourteenth day the dulness was much the same and vocal fremitus was more marked. On the eighteenth day there was still diminished expansion on the right side, tympany over the upper right front and dulness throughout the axilla and back. Vocal fremitus now seemed about normal. No tubular breathing could be made out. The temperature reached normal on the twenty-sixth day and the patient's general condition was excellent. There was still dulness in the lower right back and axilla, the vocal fremitus seemed to be slightly below normal and the breath sounds were feeble, but there was no tubular breathing and no râles. The condition in the lung gradually cleared.

It seems important to realize the frequency with which a condition somewhat like this was found with dulness, diminished vocal fremitus and suppressed breath sounds, and it is certainly not easy to see how any diagnostic rules can be given from the study of the physical signs. Practically only one thing excludes empyema, and that is the negative results of exploratory puncture. The importance of repeated exploratory tapping cannot be emphasized too strongly. In another patient, showing much the same signs, we put in a needle a number of times from the sixteenth to the twenty-third day, there being dulness, decreased vocal fremitus and feeble breath sounds. On the thirty-second day a friction rub appeared, after which the needle was again used with negative results. On the forty-fifth day there was diminished expansion, diminished vocal fremitus, dulness and very distant tubular breathing. The negative results of the punctures argued against empyema and this was borne out by the fact that clearing subsequently occurred rapidly. By the fifty-sixth day the lung was practically clear.

(b) *Tuberculous Pneumonia.*—The possibility of being entirely wrong in regard to the disease is one which must always occur in dealing with delayed resolution. The picture of acute lobar pneumonia may be given by a tuberculous pneumonia and no suspicion of the true state of affairs be entertained until the long persistence of the signs arouses suspicion. One case in this series illustrates the difficulties:

The patient had a rather mild attack of pneumonia. The termination was by lysis and with it the general condition improved somewhat, but she continued to feel very weak and suffered from severe cough. Owing to a tuberculous family history the patient was especially apprehensive about

her condition. On the thirteenth day there was still quite marked diminished expansion on the left side, with dulness over the lower lobe, increased vocal fremitus and very marked tubular breathing. By the forty-second day the tubular quality was somewhat less marked, otherwise the signs were much the same. Repeated examinations of the sputum for tubercle bacilli were negative. The patient's general condition did not improve and very severe cough continued. By the end of the seventh week the dulness was less marked and the tubular quality of the breath sounds was less distinct. By the end of the ninth week the physical signs of consolidation had practically disappeared and after this the general condition improved rapidly and the cough ceased. The leucocytes throughout were not increased, being generally between 7000 and 8000. There do not seem to be any means by which a definite opinion could have been arrived at in such a patient, say a week after the termination of the pneumonia.

The tendency is more often to regard a tuberculous condition as delayed resolution than the reverse. There is no physical signs or combination of physical signs which can be regarded of great value. Enough has been said of the great variation in delayed resolution. The general condition may be of some aid, for as a rule with tuberculous pneumonia this does not improve, but the reverse. Often in delayed resolution, despite the persistence of the condition in the lung, the patient improves and gains weight, which speaks against a tuberculous process. But by far the most important aid is the daily systematic examination of the sputum. Tubercle bacilli may be found early, but commonly not until the second week at least. Persistent negative findings must be considered as one of the most important points against tuberculous pneumonia. The possibility of delayed resolution after lobar pneumonia occurring in a patient who has a previous tuberculous lesion must be kept in mind. A lobar pneumonia (not tuberculous) in a patient with pulmonary tuberculosis is not uncommon and there is no reason why delayed resolution should not occur. It would be difficult to arrive at the correct diagnosis until time made it for us.

(c) *Extension of the Pneumonia.*—It is possible that very slow extension of the consolidation, after the main features of the attack are over, which does occur rarely, might give difficulty. However, a careful examination from day to day should prevent the mistake, and clearing is usually present in the part of the lung first affected.

(d) In some cases the question of what has been termed a chronic pneumonia may arise. The term is applied to various conditions which do not differ anatomically from delayed resolution, or at any rate

from the changes which may persist after it. There is some question as to whether we may have chronic pneumonia which has not followed delayed resolution. As far as physical signs go, it would not seem possible to separate it from delayed resolution. In a patient coming under observation at a late stage, the history is the greatest help in making the diagnosis.

*Prognosis.*—This has to be considered as regards life and as concerns the end result in the lung. Concerning the former, delayed resolution involves but little danger to life. In this series two patients died, but of other conditions, one having an empyema with a purulent pericarditis, the other having endocarditis. Regarding the restoration of function there is more question. Judging from the physical signs in the great majority of this series the patients were discharged in good condition. The exceptions were patients who felt perfectly well and insisted on going home before the signs had entirely disappeared. The majority showed only dulness on percussion, two having slightly suppressed breath sounds. However, when we remember that in one of the cases coming to autopsy there were definite changes in the lung within twenty-five days of the onset of the pneumonia, it seems reasonable to suppose that some alteration is probably common in patients who recover with little apparent change. In one case, already quoted, there were distinct signs of drooping of one shoulder and asymmetry of the chest by the forty-sixth day. It would be interesting to have reports of the changes found at autopsy years later in persons who had delayed resolution. As to the duration of the condition, the lung was clear in the fourth week in 5 cases; in the fifth week in 10 cases; in the sixth week in 4 cases; in the seventh week in 9 cases; in the eighth week in 4 cases; in the ninth week in 3 cases; in the tenth week in one case; in the eleventh week in one case; and in the twelfth week in one case.

*Treatment.*—In this it is evident that we should have the patient under the best possible general conditions. He should have abundance of fresh air, being kept out of doors, if possible, and given all the nourishing food he can take. There does not seem to be any reason, if his general condition permits of it, why the patient should not be allowed to sit up in bed, or, if there is not much fever, even allowed up in a chair. It seems, however, of doubtful propriety to allow the patient to get up and go about.

When we consider the condition of the lung in delayed resolution the slight chance of influencing it by any drugs seems evident. Expectorants cannot be expected to do so, although they may render the cough less trying. Codeia and heroin may be given to allay a troublesome cough and the former drug may be helpful in easing pain if it be present. Potassium iodide and some form of mercury are given, but it must be confessed rather with hope that they may help than certainty that they will. At any rate their use can do no harm. There is no drug which will, so far as we know, certainly influence the ferment activity. That blisters to the thorax can have any influence seems doubtful. In the use of any therapeutic measures we must remember how rapidly a lung may clear without any treatment and hence be cautious in attributing results to some measure which has been adopted.

The influence of the X-rays on metabolism suggested the value of their influence in delayed resolution. This has been fully discussed by Edsall and Pemberton.[1] They point out the importance of using this treatment only for patients in whom all signs of inflammatory progress have disappeared. At the same time it is evident that the process must not have continued until marked changes in the lung have occurred before the X-rays are used. As already noted these may come on comparatively early. That the condition is actually delayed resolution should be determined beyond doubt, for a patient with tuberculous pneumonia would probably be harmed by exposure to the rays. Edsall and Pemberton emphasize the fact that it should always be realized that there are dangers in this method of treatment and that care in regard to the duration and degree of exposure should be the rule.

There were not enough cases in this series treated by the X-rays to enable any conclusion to be reached. The exposures were usually given to the number of four, on alternate days and for a period of about five minutes. There seemed to be good results in the patients so treated; some cleared with rapidity. However, until a large number of cases are available, one can only give general impressions and not definite statistics. The effect on metabolism was very marked in the cases reported by Edsall and Pemberton.

[1] American Journal of the Medical Sciences, 1907, CXXXIII, p. 286.

*Conclusions.*—The study of this series suggests the following conclusions:

1. That the factors usually considered to be of importance as affecting the occurrence of delayed resolution, such as apical involvement, advanced age, debility and cachexia, did not seem to have any influence.

2. As regards age, three-quarters of the patients were between the ages of seventeen and forty years.

3. The conditions which did seem to affect the incidence especially were (a) color and (b) involvement of the right lower lobe. The colored showed a relative high incidence as compared with the white race. The lower lobe of the right lung was concerned much more frequently than any other, both in the total number of cases and relatively in proportion to the number of cases in which it was involved in the pneumonic process. The cause of this is obscure unless it be diminished movement on account of the relationship to the liver.

4. The physical signs show great variation and no general description can be given of them. This applies both to the signs during the continuance of the delayed resolution and during clearing.

5. The diagnosis must frequently offer difficulty and can often only be made by exclusion of other possibilities. Empyema and tuberculous pneumonia are the conditions which give the greatest difficulty.

6. As regards prognosis, while the danger to life is not great, it is never safe to predict absolute restoration in the lung. Permanent change may appear in a short time.

7. The use of the X-rays is the most hopeful therapeutic measure, but these must always be used with caution and only after the diagnosis is positive.

# SKIN TRANSPLANTATION.

## With a Review of 550 Cases at the Johns Hopkins Hospital.

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This paper is based on a study of the literature, and my own personal clinical and experimental observations, and also includes a critical review of 550 house cases which have been skin-grafted in the clinic of Dr. Halsted, at the Johns Hopkins Hospital. In this series all types of grafts have been used, and skin defects on almost every part of the body have been grafted.

I take this opportunity of thanking Dr. Halsted for his encouragement and suggestions in the preparation of this paper.

*History.*—Long years before skin grafting was attempted in Europe or America, certain individuals of the Tile-makers caste in India obtained wonderful results in plastic operations with pedunculated flaps from the forehead or cheek for the repair of amputated noses, and occasionally used successfully sessile flaps including the subcutaneous fat taken from the skin of the gluteal region, after it had been beaten with wooden slippers until considerable swelling had taken place. They used a secret cement for the adhesion, to which was ascribed special healing power. This method is called the Ancient Indian method.

It is interesting to note that plastic surgery was practiced in ancient India and Egypt, as has been shown by the sacred writings of India and in Ebers' Papyrus, both of which mention rhinoplasty as a well-known procedure.

Celsus speaks of the restoration of ears, noses and lips, by the aid of the neighboring skin, and Galen, Antyllus and Paul of Ægina also mention these operations.

In 1597 Gaspar Tagliacozzi published in Venice, in two volumes, the first systematic work on plastic surgery.

He describes minutely the several operations, giving special prominence to his original method of rhinoplasty, in which the whole-thickness living flap is obtained from the arm. This is called the Tagliacotian or Italian method, in contradistinction to the Indian or Oriental method, and is the basis of the operation in use to-day.

Early in the nineteenth century, Baronio, the physiologist, speaks of two interesting cases, one of which he saw himself, and the other which was related to him by Dr. Saucassani, as follows: A female charlatan, Gamba Curta by name, in order to show the efficacy of an ointment she was selling, cut a piece of skin from her thigh, and after passing it around for inspection, replaced it in its original bed, and dressed it with the ointment. The next evening, it was so far healed that no further dressing was necessary. The exhibition that he saw himself he relates as follows:

In the little village of Rovate, a charlatan was selling an ointment which he claimed was good for every trouble, and which he named the ointment of the French Army. Baronio suggested to him that the power of the ointment would be much more manifest if he would cut a piece from his own arm. He did this, cutting a large piece of skin from his forearm, including some of the underlying muscle, and after holding it up for the spectators to see, replaced it, and dressed the wound with his ointment. Eight days later, at the same place, he exhibited his arm, and the scar of the wound could scarcely be seen. These two cases suggested to Baronio the following experiments, which he carried out on sheep, in 1804.

In the first experiment, two whole-thickness pieces of skin of equal size and exclusive of the subcutaneous tissue, were cut from either side of the root of the tail of a sheep, and were immediately transferred to opposite sides. The second experiment was similar, except that the pieces of skin were kept detached 18 minutes. In the third experiment, larger pieces were used, 5 x 3 inches, including cellular tissue and a bit of muscle. These were detached one hour, before being transferred to opposite sides. All of the above-mentioned experiments were successful, and the grafts bled when cut into, 10 to 12 days after the transplantation.

Carpue, in London, in 1814, first successfully performed rhinoplasty by the Indian method, with the sessile flap, and Bünger in Marburg, in 1823, was also successful with this method.

Graefe did not succeed with his attempts at rhinoplasty with sessile flaps, and Von Walther, Diffenbach and Wertzer were scarcely more successful.

In spite of these discouraging results, other surgeons continued to experiment from time to time with varying success. Von Langenbeck says: "It was thought in former times, especially when science was governed by natural philosophy, that even after a piece of skin had firmly grown to its new owner, its nutrition depended on the state of health of its original possessor." Fortunately we now know this is an erroneous theory.

Frank H. Hamilton, on January 21, 1854, in the Buffalo General Hospital, raised a whole-thickness pedunculated flap, 4 x 7 inches, from the calf of a man's leg, for the relief of a large traumatic ulcer of the other leg. This flap was held away from its bed by dressings, and remained viable, although there was considerable shrinkage. After two weeks he freshened the under surface and edges of the flap, excised the ulcer and part of the cicatrix, then partly covered the wound with the flap, and secured the legs together. Two weeks later the flap was amputated from its base, and a portion of it subsequently sloughed. It is interesting to know that 10 years before this operation was performed, Hamilton had suggested this procedure for the relief of an ulcer of the thigh, but was unable to obtain the patient's consent. He recognized the important fact that if a graft is smaller than the chasm which it is intended to fill, it will grow or project from itself new skin to supply the deficiency, and therefore it is not necessary to make the graft so large as the defect to be covered. Little general notice was taken of Hamilton's report, however.

Xetolitzki, on April 11, 1869, successfully transplanted small elliptical-shaped pieces of whole thickness skin from the back of the patient's hand in the treatment of a case of avulsion of the scalp.

The communication of J. L. Reverdin to the Society of Surgery in Paris on December 8, 1869, in which he showed a patient on whom he had practiced "epidermic grafting" with small bits of skin, on a granulating surface, attracted universal attention, and gave great stimulus to the subject of skin grafting throughout the entire world.

He obtained his idea by observing the epithelial growth from a spontaneous island in an ulcer case. He said that the living epidermis was alone necessary for the success of the graft, and that the transplanted epidermis caused the transformation of the embryonal cells

of the granulation tissue into epidermic cells. Bryant, on the other hand, declared that the grafts themselves grew, and that there was a spread of epithelium from the graft, and this view has been proved correct, as it is now a well-known fact that epithelium is only derived from pre-existing epithelium.

Pollock, in 1870, reported several successful cases done by Reverdin's method, to the Clinical Society, of London. His grafts were very small, and were cut with scissors.

George Lawson, at the same meeting, presented cases in which he had used successfully pieces of epidermis as large as a sixpence, which he also cut with scissors. He mentioned the possibility of very much larger grafts being cut, but did not attempt to cut them himself. Both of these men placed their grafts on untouched granulating areas.

Ollier, in 1872, grafted large areas of skin, 4, 6 and 8 cm. sq. in extent, using the whole-thickness of the dermis, instead of the small bits of epidermis of 2 to 4 mm. sq., as advised by Reverdin. His idea was not to create multiple centers of epidermization, but to substitute for the ordinary healing a surface having the essential elements of the normal skin surrounding it, and also to preserve its characteristics. This idea was a distinct advance and is the object aimed at to-day.

LeFort, in February, 1872, successfully transplanted from the arm, for the relief of an ectropion, a sessile whole-thickness flap, from which the subcutaneous fat was removed.

Thiersch, in 1874, transplanted whole-thickness pieces of skin 1 cm. in diameter, from which the adipose tissue was carefully removed. He laid great stress upon the following facts, that, upon perpendicular sections of the granulation tissue one can easily distinguish upon the deeper part quite dense connective tissue, and a vascular net-work in a horizontal position. From this horizontal vessel and tissue layer sprouts the much softer and more vascular true granulation tissue, "granulation caruncle." If the possibility is taken from this soft vascular "granulation caruncle" of not changing into a firm cicatrix, then the graft over it will sooner or later break down. Therefore, nothing remained but to exclude the superficial part of the granulations from the procedure, and to graft the skin immediately upon the lower horizontal ground. This has also been proved a fallacy.

He said that the agglutination took place within a layer of subcutaneous cement substance. The agglutination, if entirely successful,

resulted under the inoculation of the vessels which could be seen in 18 hours, *i. e.*, the connection between the vessels of the granulation tissue and the applied skin ensued, through intercellular ducts, filling the same immediately with blood from the granulation vessels, which blood circulated in the vessels of the applied skin.

Also the vessels of the transplanted skin were liable to a secondary change in which they approached for a while, more or less, the structure of the granulation vessels.

In some cases only the lower part next to the connective tissue adhered, while the upper layer was cast off as a scab. The sweat glands were in this under layer.

In 1875, Wolfe, of Glasgow, reported a successful plastic operation for the repair of a defect about the lower eyelid, with a sessile flap from the arm measuring 1 x 2 inches, from which all the subcutaneous fat had been removed, and he is generally accredited with introducing this method, and with insisting on this important step in the operation, although LeFort had done the same thing in 1872. Thiersch, in 1874, had also successfully transplanted small whole-thickness grafts from whose lower surface the adipose tissue was carefully removed.

In 1886, Thiersch demonstrated his method, which has revolutionized skin grafting. He showed that the healing of a fresh or granulating wound of whatever size could be brought about more quickly by covering the defects with large films of epidermis in connection with the stratum papillare of the cutis.

Krause, in 1896, reported his perfected technic for the transplantation of sessile whole-thickness flaps, to or from any part of the body. He found that skin from any location could be used after the removal of the subcutaneous fat, and the less it was maltreated the better. This method is advisable in exposed positions where more resisting skin is required than is given by Thiersch's method.

In 1905, Young, of Glasgow, in a very interesting paper, modified Krause's technic. The important points in these methods will be discussed in detail later.

Hirschberg claims that it is necessary to produce a sort of plethora in the cutaneous flap before it is excised, and this may be accomplished by beating it with rubber tubing, thus repeating to a certain extent the old Indian method. He also thinks that only the skin with a very dense vascular net-work should be used, and says it is not necessary to remove the subcutaneous fat.

I reported a case in 1907 in which I successfully transplanted a sessile flap on which a considerable portion of the subcutaneous fat still remained, and similar cases have been reported by other surgeons, but this procedure is as a rule not as successful as when the subcutaneous fat is entirely removed.

*Definition.*—By skin grafting we mean the transplanting of either the whole-thickness, or a portion of the thickness of the skin, from one part of the body to another, for the purpose of closing a breach of surface in the skin, in order to hasten its healing process, and to prevent, as far as possible, future cicatricial contraction. This may be done immediately on a fresh wound, or after repair has set in.

*Classification.*—Grafts may be divided in general into *thin grafts*, where only a portion of the thickness of the skin is utilized, as obtained by the methods of Reverdin and Thiersch, and *thick grafts* where the whole thickness of the skin is used. This latter division includes whole-thickness sessile flaps, and whole-thickness pedunculated flaps, from distant parts, with subsequent amputation of the pedicle. Grafts may be further classified into: *autodermic*, where the graft is obtained from the same individual; *isodermic*, where the graft is obtained from another individual of the same species; *zoödermic*, where the graft is obtained from a lower species.

The majority of grafts are autodermic, although excellent results are secured from grafts obtained from amputated limbs and cadavers within a few hours after death due to accident. The skin of still-born children has also been utilized. I have used with success many elliptical-shaped pieces of whole-thickness, taken from the lax abdominal skin at laparotomy operations.

### Methods of Obtaining Thin Grafts.

*Reverdin's Method.*—Reverdin usually obtained his small bits of epidermis from the inner surface of the leg. He held the skin tense over the flat surface of the tibia, and introduced the point of a rather large venesection lancet parallel to the bone, and to the depth of .5 mm., then pushed it forward so that the point should emerge 3 or 4 mm. further on, the small piece of epidermis being cut loose by the edges of the lancet, and he adds that the little wound is the seat of a fine sanguineous dew. He placed the lancet bearing the graft upon the healthy granulations, and slid it off, raw surface down, with the point of a pin, taking care that the edges were not rolled under. After all

the grafts were placed, usually in rows, he covered them with strips of plaster which were not disturbed for 24 hours. Another simple method of obtaining the minute pieces of epidermis is that of Agnew, who transfixed a bit of the superficial layer of the skin with a sewing needle held in an artery clamp, and raised it to form a cone, then with a razor or sharp scalpel cut off the tip of the cone and transferred it on the needle to the desired point. Smith's scissor forceps were also used for cutting these grafts (Fig. 1). At one time it was thought neces-

FIG. 1.—Smith's scissor forceps for cutting Reverdin grafts. With the blades open the small mouse-tooth forceps pick up and hold firmly a bit of the superficial epidermis, and this is cut off on closing the blades.

sary to insert the grafts into a small incision in the granulations, and another method was to force the grafts into the granulations with a small blunt instrument. However, these latter were soon abandoned for the simple procedure above described. As these grafts are obtained without pain, and are applied to the granulations without disturbing them, anesthesia is unnecessary. This method gives numerous small epidermic islands from which the new epidermis will spread to fill the gaps between, and finally meet the stimulated epithelium from the edges of the ulcer. These grafts are as a rule applied only to undis-

turbed granulating surfaces. There is more liability of future cicatricial contraction following this method than from the methods to be described later. A very large number of Reverdin's grafts have been used on some cases. On Abbe's case of avulsion of the scalp 14,000 minute grafts were used during a period of 4 years.

Another method of obtaining small thin grafts, giving good results, is to remove with a sharp scalpel the narrow, opalescent growing edge of newly formed epithelium along the margin of a healthy granulating area. Transplant the strip of epithelium onto the granulations at a distance from the edges of the wound, either in a single piece, or cut into small bits. It may also be used as a pedunculated flap. This can be done with no pain to the patient, and is generally successful, inasmuch as new islands of epithelium are formed wherever these grafts are placed. Souchon described this method in 1909, but it has been used by various surgeons for a number of years.

*The Thiersch Method.*—Thiersch's original instructions in 1886 were to cut or scrape off the granulations down to the firm underlying tissue, and to stop all hemorrhage thoroughly. He considered that the skin to be grafted was best obtained from the outer surface of the upper arm, which was put on a stretch with one hand, while with a razor very thin films of skin were cut by a sawing motion. He said that even the thinnest films obtained in this way included in addition to the superficial epidermis the papillary layer, as well as a portion of the reticular layer, of the corium. He was able to cut and successfully transplant pieces 10 x 2 cm., and thought it necessary to transplant directly on the firm base and not on the unstable soft granulations. He advised that such grafts also be used on fresh wounds, and skin defects following operations and injuries, and thought this method especially valuable for the relief of ulcers following burns. At first he applied the grafts with spaces between each strip to allow the escape of the secretions, but later the strips were placed slightly overlapping each other, and the skin edge, and thus secondary contraction of the mosaic-like scars was avoided. Wet salt solution dressings were used, care being taken that no antiseptics should come in contact with the grafts.

Socin, in 1888, used a microtome knife for cutting these grafts, and thus was able to obtain longer and broader films; some of his grafts from the thigh measured 20 x 5 cm. Thiersch considered this a distinct advance in technic.

### The Technic at the Johns Hopkins Hospital for Thiersch Grafting.

*Preparation of the Skin from Which the Graft is to be Cut.*—Shave the selected area and scrub carefully with green soap and water, and rinse with water. Sponge with ether, follow with 70 per cent alcohol; then with Harrington's solution (bichloride of mercury 9 grains, hydrochloric acid 60 cc., alcohol 600 cc., water 330 cc.), and finally

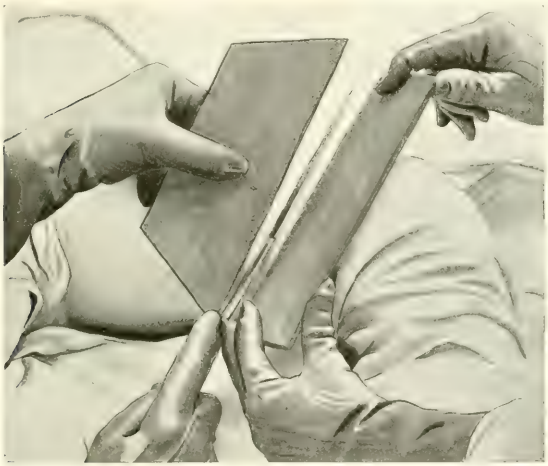

Fig. 2.—The boards in place holding the skin of the thigh flat and taut. The edge of the Catlin is engaged in the skin. (Photograph by Schapiro.)

wash thoroughly with a bichloride of mercury solution 1-1000. Again wash carefully with sterile normal salt solution, and apply a sterile gauze dressing wet with normal salt solution until ready to cut the graft. (When Harrington's solution is omitted use 95 per cent alcohol and continue as above.) The grafts are almost always cut from the thigh, and usually from the right one when practicable. The anterior and inner portion is the first choice, the external aspect next, and finally, if necessary, the posterior portion. Occasionally the skin from the arm or leg is used.

*Cutting of the Graft.*—Place a small sand bag beneath the thigh in order to give a better surface from which to cut. Arrange the usual sterile dressings about the selected area. Care must be taken that no carbolic or bichloride solutions be brought into the field, or touch the grafts, either on the dressings, gloves or instruments.

The Catlin knife and the boards after being boiled are placed in salt solution, and the sterile rubber protective is removed from the bichloride solution, and also put in salt solution.

FIG. 3.—The cutting is nearly completed. The graft is held up by an instrument. The fine punctate bleeding from the tops of the papillæ can be seen. (Photograph by Schapiro.)

Firm traction is exerted on the limb. The skin, wet with salt solution, is then put on the stretch, and held as flat as possible by means of two sterile boards about 8 inches long, placed quite close together at right angles to the length of the limb, the first being held by the assistant, and the other by the left hand of the operator.

The edge of the thin, sharp Catlin is then engaged in the skin between these boards and held almost flat against the limb (Fig. 2), and by a rapid sawing motion the graft is cut, the knife closely follow-

ing the board in the hand of the operator, which is drawn slowly along in front of it (Fig. 3). The graft is cut at a level, which will include the tops of the papillary layer of the corium, and only a slight amount of bleeding will follow.

After cutting the graft, it is picked up, with the raw surface exposed, upon a piece of protective taken from the salt solution. The whole is then placed upon a board and by means of a smooth instrument the graft is spread out evenly (Fig. 4). It is then covered with gauze wet in salt

FIG. 4.—Shows the area from which this small graft was cut. The graft is being spread out on rubber protective, raw surface up (Photograph by Schapiro.)

solution until the area to be grafted is ready. For several years the large grafts on the defects following operation on breast cases have been button-holed here and there on occasions, to get rid of air bubbles. I believe that every Thiersch graft over 3 cm. in diameter should be button-holed here and there, to allow the escape of secretions, and in my own work I carry this out as a routine measure, with very satisfactory results.

*Application of the Graft.*—Being sure that all bleeding has ceased, the protective on which the graft is spread is placed over the defect so that the graft is next to the wound. Then gradually the protective is lifted up and the graft is separated and left in place. It is pressed down evenly on the wound with pieces of gauze in order to get rid of any air bubbles, and to make it adhere as closely as possible. Should more than one graft be needed, they are placed so that they overlap a little the edges of the wound and the adjacent grafts.

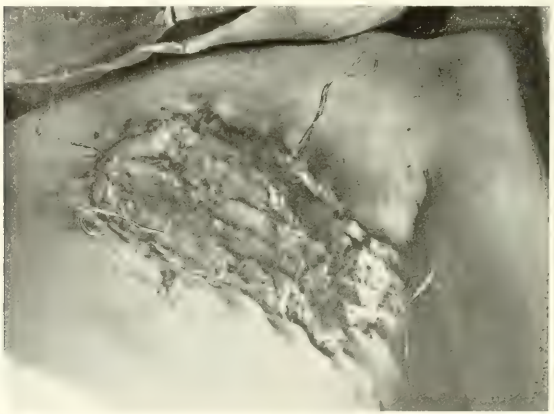

FIG. 5.—Complete take, Thiersch graft, on a breast wound at the first dressing, 10 days after grafting. Silver wire pucker sutures can be seen in the skin edge.

*Preparation of the Surface to be Grafted.*—If the graft is to be applied to a clean, fresh wound, it is important to see that all hemorrhage has ceased, and that the wound is as dry as possible. If a granulating wound is to be grafted, it is only necessary that the granulations be in a perfectly healthy condition before the grafting is attempted.

In a few cases the grafts have been applied directly to the healthy granulating surface after cleansing this surface as thoroughly as possible with irrigations, gauze pledgets and wet compresses, being careful not to cause any bleeding. My own experience has convinced me that

Thiersch grafts of whatever size will take just as well, if not better, upon a healthy granulating surface as upon a fresh wound. Lauenstein's method of rubbing off the granulations with sterile gauze tampons has also been used, but usually the granulations were thoroughly removed with a stiff nail brush, a curette or a scalpel, down to the firm base, and the grafts applied. In addition to the above, in some cases

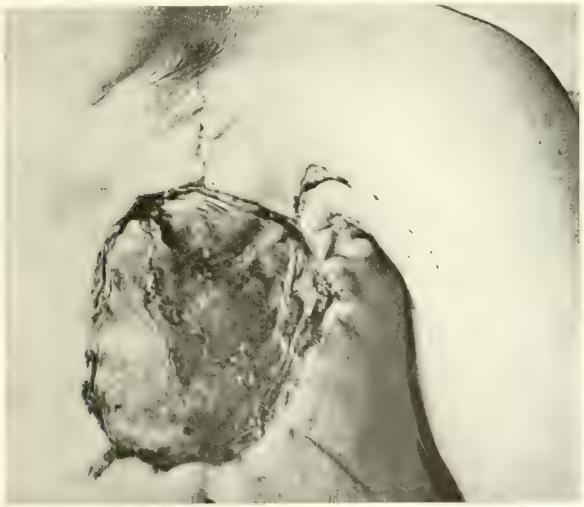

FIG. 6.—Complete take. Thiersch graft, about 2½ weeks after operation. The graft has flattened down and joined the skin edge.

the unhealthy skin edges were excised and gridiron incisions made through the hard, fibrous base of the ulcer to healthy tissue beneath, extending out into the normal surrounding skin, in order to obtain a better blood supply. In some old, chronic ulcers, the entire ulcer, including edges and base, were excised down to healthy tissue, and the graft applied.

By the method above described, the largest and most satisfactory grafts can be cut, but this requires a skillful hand and constant prac-

tice, so consequently this method cannot be recommended generally. It is desirable then that some simple method of cutting be found which can be used in hospitals, and also be employed by practitioners who may have an occasional call for a skin graft. It would seem best, therefore, to use a guarded knife or razor of some sort for the cutting, whereby the thickness of the graft can be accurately regulated without much practice. By this means grafts with even edges and of any desired width can be cut, depending on the length of the guarded blade (Figs. 5, 6 and 7).

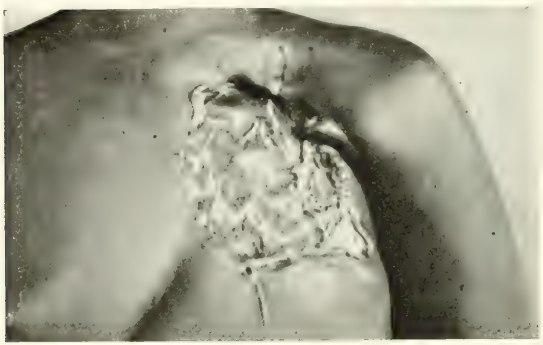

FIG. 7.—Healed graft which is firmly adherent to its bed.

*Skin Grafting for Chronic Roentgen-Ray Dermatitis.*—Dr. Charles A. Porter, of Boston, at the ninth annual meeting of the American Roentgen Ray Society, held in New York, December 28-30, 1908, said in part as follows: "There is always a time when the chronic Roentgen-ray lesions can be successfully eradicated by minor operations, but neglect has led to the necessity for major operations, in spite of which metastases and death will occasionally occur. No other agent is so potent in the production of multiple carcinomata in man. The most important changes are the rarefaction beneath the epidermis, with a total loss of papillæ and a telangiectatic condition of the blood vessels, disappearance of the glands, obliteration of the arteries and great increase in the connective tissue. The epidermis is thin and

atrophic, with foci of epithelial proliferation, in some instances giving rise to papillary down-growths with keratosis, and in others to the invasive type of new growth. Apparently, the repeated exposures to the ray produce chronic changes in which the normal reparative power is lost. There is no constant change in the nerve trunks. In some instances the nerve fibers are replaced by connective tissue, and the nerves are compressed by the dense cicatricial tissue about them. This perineuritis may explain the extreme pain so characteristic of the lesion in the majority of cases. Of 44 cases recorded in the literature, 11 of which came under my observation, 6 were severe lesions of the ulcerative type, 4 beginning epithelioma and 34 undoubted carcinoma, with 8 deaths, a mortality of 25 per cent. There is always a latent period, usually one of years, and either keratosis or ulceration precede the cancer. The only treatment which will prevent trouble is early removal by caustics or the knife of all suspicious lesions. When occurring on the backs of the hands, the lesions may be excised and the wound sutured, or destroyed by liquid air or by carbon dioxid snow. When keratosis or ulcerations occur on the dorsal aspects of the fingers, and especially when the skin is dense, I advocate excision and skin grafting. If the primary grafts do not take, owing to inadequate blood supply, the surface may be covered with grafts later, when connective tissue has formed. Healing by cicatrization sometimes occurs, but owing to the thinness of the epidermis and the liability to subsequent injuries, skin grafting is preferable. Moderately thin grafts take better than thick ones. Hemorrhage should be controlled before the application of the grafts, and pressure must be maintained for 24 hours."

*Technic.*—(Described to me by Dr. Baetjer from his personal experience.) Under ether, after applying a finger tourniquet, excise the suspicious areas, then remove the tourniquet, and check all hemorrhage by pressure with dry gauze. Elevate the hand and expose to the air. Bevel the edges of the wounds as far as possible, and cut small Thiersch grafts which are thickest in the middle and gradually become thin toward the periphery. Place them on the fresh wounds so that they do not overlap the skin edges or each other. Dress with rubber protective which extends about $\frac{1}{8}$ of an inch beyond the margin of each graft, and over each put a small dry gauze pad. Apply direct down-

ward pressure on every graft separately, with a bandage, and secure underneath the part. The hand is immobilized on a splint (sometimes before the grafts are applied), and then is elevated so that it is always higher than the elbow. This is a most important point in the technic, and the elevation is continued for at least two weeks.

The first dressing is made from 24 to 36 hours, when the protective is removed and the grafted area carefully examined to ascertain if there is any collection of serum or blood beneath it, in which case it is snipped, and the graft pressed back in its bed. All lateral movement of the graft must be avoided. The edges of the graft are then covered with a thin coating of lanolin, or of the following ointment which is less macerating—citrate of silver, ½ grain, ichthyol, 5 grains, benzoinated lard, 6 drachms, lanolin up to 1 ounce.

The proportion of lanolin in the ointment is varied according to the case, less lanolin being used if the hand is moist and soggy, more if the skin is too dry. The hand still on the splint is now put in a wire cage, and exposed to the air. On the 4th or 5th day it is thoroughly soaked in salt solution in the morning and evening, and the grafts examined, as by this time their vitality can be determined. Any necrotic portions are clipped off, and exuberant granulations are touched with nitrate of silver. After two weeks in the cage, dress as an ordinary wound.

Dr. Porter finds that autodermic grafts are more apt to take than isodermic, and has developed this technic, with which he has been most successful in all X-ray cases. These cases bring up problems which are very different from those presented in skin grafting on ordinary wounds, and the technic is of great value.

Many special knives and instruments have been devised for the cutting of grafts, among which Mixter's rectangular fenestrated curved plate may be mentioned. On the under surface of this plate is a row of sharp needle points which serve to keep it in place. The outer edge of the plate is quite thick and gradually tapers off until the window is reached where it is very thin. The skin of the thigh is stretched, and the plate is applied. Then the roller is pressed firmly down upon it, thus flattening the skin between the thin edges of the plate, and the graft is cut by a saw-shaped knife, which follows the roller at a suitable distance. By this means thin, smooth-edged, narrow grafts, of uniform thickness, can be cut (Figs. 8, 9, 10 and 11).

FIG. 8.—Kortuem's knife for cutting Thiersch grafts. The blade is double edged and very thin. It is 16 cm. long by 1¾ cm. wide. This is a very light and satisfactory knife.

FIG. 9.—Rehn's knife for cutting Thiersch grafts. This is a very heavy, well-balanced knife. The under surface is ground flat, and on the back of the blade, nearest the handle, there is a roughening to prevent the finger from slipping. The blade is 12 cm. long by 2¾ cm. wide.

FIG. 10.—Thiersch's knife for cutting thin grafts. The single-edged blade is ground flat on both sides. The blade is placed at an angle to the handle, which is advantageous in the cutting. It is 8 cm. long by 1¾ cm. wide.

FIG. 11.—Heavy razor for cutting Thiersch grafts. One side plane. One side concave. Slide fixation.

Hoffmann uses a knife with a safety guard, and by means of screws can regulate exactly the thickness of the graft (Fig. 12).

Doolittle has had good success with an ordinary "Star safety razor," and says that no skill is required, and that good grafts of uniform thickness can be cut by this simple instrument.

Lanz cuts a long Thiersch graft and divides it, then stamps each piece with a die which cuts a row of transverse incisions down the center of the flap, with a parallel row of incisions on each side at the same time, extending from the edge about a third of the way across

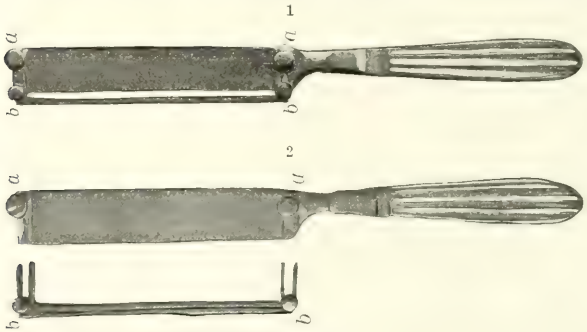


FIG. 12.—Hoffman's guarded knife for cutting Thiersch grafts. (1) Knife with guard in place. (2) Knife and guard separated. The guard is secured by two screws (*a*) which are on the knife itself. The thickness of the graft is regulated by the screws (*b*) which are on the guard.

between the central incisions. Then by taking hold of the edges of the flap, he is able to pull it out 2 or 3 times its former length. He applies one of these opened flaps to the defect to be covered, while the other piece he places on the wound left by the cutting. In this way both wounds heal rapidly and simultaneously. The small open spaces in the flap allow the escape of secretions, and soon heal.

Vogel, after Thiersch grafts are in place, cuts with curved scissors in the flap two small windows, each about 2 mm. square, in each square centimeter of surface. He uses a wet salt-solution dressing for 4 or 5 days, then dresses with an ointment. The flaps heal smoothly into place, never being lifted up by blood or serum collecting beneath them. The

little windows soon heal over, but before this takes place they allow free escape of secretions into the moist dressings which prevent drying.

Försterling, instead of making windows, cuts little flaps in the graft which allow drainage as long as necessary and do not leave spaces to be covered over.

These methods, especially those of Vogel and Försterling, which are very simple, have much to recommend them, and are well worth a trial. In fact the recognition of the necessity of allowing the immediate escape of secretions which collect under the grafts is one of the most important advances in the technic of grafting. Experience has taught me that openings should be made here and there in any graft wider than about 3 cm., whether it be thin, or of whole-thickness. Many of the partial takes in our series could have been avoided had the collections of serum and blood been able to escape through such openings.

FIG. 13.—The Catlin amputating knife, which is used at the Johns Hopkins Hospital for cutting Thiersch grafts. It is double edged, and the size most commonly used has a blade 17 cm. long by 1½ cm. wide.

In old Thiersch grafts there is often a blotchy brownish, irregular pigmentation, and also a definite shriveling of the surface. Occasionally there is a contraction under a Thiersch graft which I have never seen occur under one of whole-thickness. Many Thiersch grafts are closely adherent to the underlying tissues, although sometimes they become movable later; this is in marked contrast to the whole-thickness grafts, which are much more movable; however, such adhesion is not so marked if they are placed on undisturbed granulations. In positions where the grafted area is exposed to constant trauma, these thin grafts are contraindicated.

McBurney introduced broad sharp retractors which held the skin flat and tense while the graft was being cut between them.

Two pieces of splint board and a double-edged Catlin amputating knife, which is worn thin by frequent sharpening, are all the apparatus required for cutting grafts as large as may be desired (Fig. 13). I have found the use of a single-edged blade, broader and thinner than the Catlin, more satisfactory with these boards. Thiersch grafts are

those most commonly used, and are of enormous size in comparison with those advocated by Reverdin. They can be applied to any tissue having a sufficient blood supply, to a fresh wound, to the untouched surface of healthy granulations, and to the firm base after the granulations have been removed.

Success depends on absolute asepsis. It is important that the grafts be cut of equal thickness, and include a portion of the stratum papillare of the cutis. All hemorrhage must be checked before the grafts are placed, and this can usually be done by pressure, hot compresses, peroxid of hydrogen or adrenalin. No antiseptics must be allowed to touch the grafts.

Parallel incisions, only partly through the skin, to make the lateral boundaries of the grafts, may be made one or two inches apart. Fischer made the interesting observation that grafts take best which are obtained from, and transplanted upon, parts which have been previously rendered anæmic by the use of a rubber bandage. This suggestion, however, has not been generally adopted.

It was at one time thought that skin taken from a part corresponding exactly to the defect would heal better, but this has been disproved.

In cutting grafts it must be remembered that elastic shrinkage takes place at once, and that cicatricial shrinkage takes place later. There is no way of anticipating or preventing the secondary contraction which sometimes follows an apparently successful Thiersch grafting, the cicatricial tissue forming under and between the grafts. McBurney thinks it is due to the too early abandonment of wet dressings, but there do not seem to be any more of these cases where dry dressings alone are employed than where wet dressings are used throughout. The wound from which the graft is cut usually heals promptly, and leaves only a slight scar (Fig. 14). The general health of the patient is as a rule important to successful transplantation. Grafts do not take as well on syphilitic patients, and care must be taken in isodermic grafting not to transmit disease to a healthy person, as cases have been reported in which small-pox, syphilis and tuberculosis have been transmitted in this manner.

Absolute contact is necessary and this is usually obtained by pressing the graft firmly into its bed with gauze. Wight suggests sealing the graft to its base with the high frequency current, but this is unnecessary for success.

Ballance, in grafting the cavity left by a radical operation for

chronic middle ear disease, obtains absolute contact by means of suction with a very fine pipette, which extracts the air, and the graft is pushed in by atmospheric pressure. This method might be used to advantage in causing the desired contact in other larger, deep cavities requiring a skin graft.

Accurate placing of the grafts minimizes the scar, and thus prevents to a certain extent secondary contraction. Immobilization of the part after grafting is important.

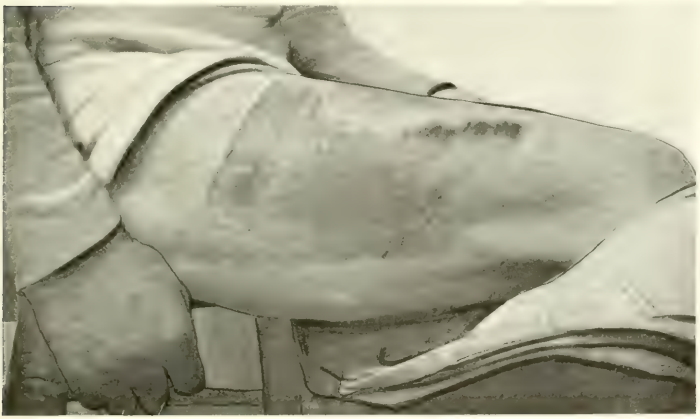

FIG. 14.—Scar on outer side of thigh due to cutting of Thiersch grafts. Photograph taken 5 weeks after operation.

*A Method of Splinting Skin Grafts.*—There are many partial takes and failures for the reason that the grafts are not properly splinted after they are applied, and in consequence slip down with the dressings, or are floated off by blood or serum collecting beneath them. In order to overcome this difficulty it is necessary to reinforce the grafts with some material which has enough body to act as a splint, and at the same time is not too rigid to shape itself readily to any desired location. It is also very important that it should not adhere to the grafts and granulations, or cause too much pressure, and also that there be free escape of any secretions into the dressings.

After experimenting with various materials, I tried a coarse-meshed net, such as is used for curtains. It is made of loosely woven flat bars of cotton thread, surrounding openings about 1 cm. in diameter (Fig. 15). It is necessary to have the openings approximately this size, as smaller ones often become clogged. This proved too flimsy, and also became adherent to the grafts. So in order to increase the body of the fabric, after washing out the sizing and drying, I soaked the material in a rubber solution made up of pure gutta-percha, from 15 to 30 parts

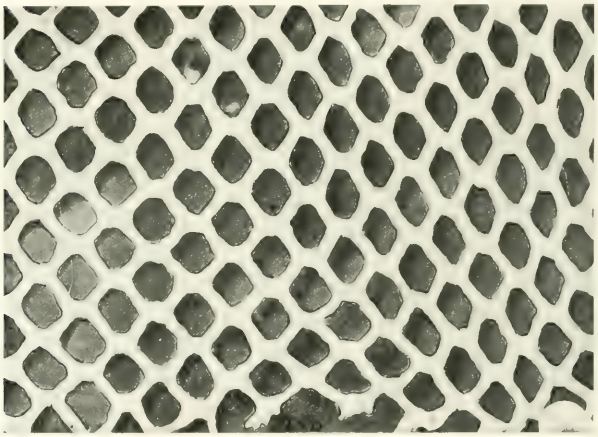

Fig. 15.—Actual size of the openings of the rubber impregnated mesh, used for splinting grafts.

(depending on the stiffness of the material required), and chloroform 150 parts, and found that after the chloroform had evaporated and the material was dry, I had a very satisfactory splinting material. When properly prepared the net should be of a light greyish-brown color throughout.

*Sterilization before Application.*—Cut in pieces as large as may be desired and separate them with one or two thicknesses of gauze. Place in a sterile jar, and fill with 1/1000 bichloride of mercury solution. Change this solution three times at twelve hour intervals, and finally

allow the mesh to remain permanently in 1/1000 bichloride solution. It can be kept for a considerable time in this way (I have used it after keeping it nine months in the bichloride solution), although it is more desirable to make up small quantities as required. The dry permeated material will keep indefinitely. No hot solutions must come in contact with the mesh during the sterilization or application.

*Technic.*—After the grafts are in place the mesh is taken out of the bichloride solution, and thoroughly rinsed with salt solution, then

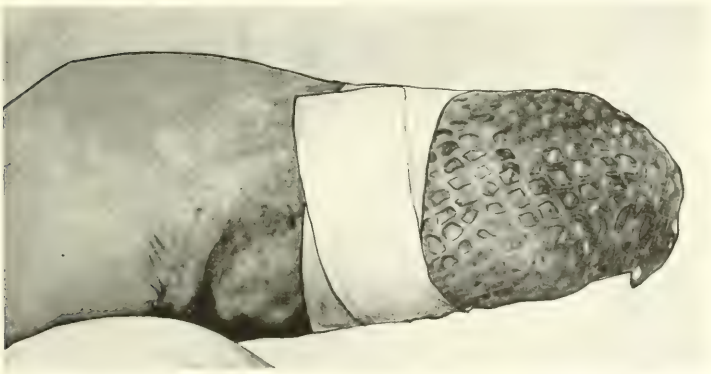

FIG. 16.—Stump covered with whole-thickness grafts, which are held in place by the rubber impregnated meshed material, secured by adhesive straps.

dried with a sterile towel. A piece is cut large enough to allow a margin around the grafted area of from 5 to 10 cm. Then the material is applied and pressed snugly down on the grafted area and surrounding skin or granulations. Should the conformation of the part or wound not permit the mesh to be evenly applied, a few cuts with scissors will allow an infolding and accurate fitting, which is necessary in order that the splinting may be successful. The overlapping edges may be secured to the skin by strips of adhesive plaster when necessary (Fig. 16). After the net is in position the dressing selected is applied, and the whole secured by a bandage.

Where the overlapping material rests on granulation tissue, it will

be found that it can be lifted up at any time without causing pain or bleeding, as the granulations do not adhere to or grow into the bars of the impregnated material (Figs. 17 and 18).

With this mesh in place the grafts can be observed from time to time with little or no danger of displacing them. Should any blisters form

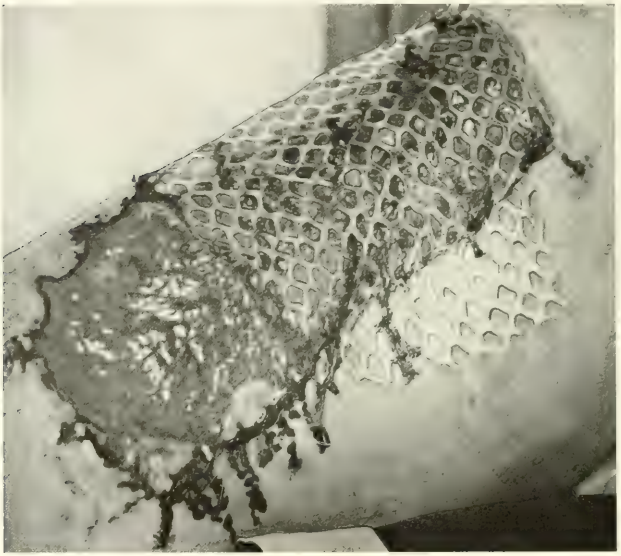

FIG. 17.—Rubber impregnated meshed material over a graft placed on the granulating wound shown in Fig. 32.

and serum or blood collect beneath the grafts, it can be removed at once. The first dressing is usually made 36 to 72 hours after operation, and if the gauze next to the mesh has dried out, it must be thoroughly soaked with salt solution, and then carefully lifted with an instrument, while with a pledget of gauze the net is held down, as the dressing is raised from it, in order to guard against any displacement. Then the wound is irrigated with salt solution, and any secretions

wiped away. The mesh is left in place from four to ten days, and then can be removed without difficulty.

Any type of dressing may be used over this material—silver foil, wet or dry gauze, etc.—and I have found it particularly desirable in those cases where the grafted area was exposed to the air.

I have used this open-meshed material over Thiersch and whole-thickness grafts on nearly every part of the body, and have found its use a distinct advantage (Fig. 19).

Perry describes a method of impregnating silk netting with parafine, for the retention of skin grafts, and reports very satisfactory results

FIG. 18.—The rubber impregnated material splinting several whole-thickness grafts on an extensive ulcer of the back.

with the material. He believes his method to be much simpler than the one mentioned above.

*Dressing of the Grafted Surface.*—Most surgeons use perforated or overlapping strips of rubber protective next to the graft, and over this, gauze saturated with sterile normal salt solution. Dry gauze is sometimes placed directly over the overlapping protective strips or directly over the graft. Some prefer alternating wet and dry dressings, while others use dry powders or ointments.

*Dressings at the Johns Hopkins Hospital.*—Since April 10, 1895, when sterile silver foil was first applied in this hospital as a dressing to the grafts, it has been used almost exclusively, and with excel-

lent results. It is put on in several layers and over this are placed the porous sheets of paper which are between the silver leaves. This dressing allows the secretions to come through to be absorbed by the gauze which is placed above it. The dressing is secured by a bandage and the part immobilized. The first dressing takes place ten days later.

Mayer makes a sort of cage by putting a ring of sterile gauze around the limb above and another below the wound; resting on these rings

FIG. 19.—A whole-thickness graft splinted by the rubber impregnated material. Photograph taken 4 days after application.

little strips of sterile wood are laid, and over this is put the wet dressing, thus making a moist chamber, and preventing pressure on the newly grafted area.

Brüning advocates leaving the grafts exposed to the open air. He claims that absence of dressings prevents displacement of the grafts, that the grafts heal within eight days, and there is no subsequent shrinkage. Also that any collection of serum under the grafts can be quickly noticed and easily pressed out (Figs. 20, 21, 22 and 23).

Goldman says of the open method that as the chief object is secure fixation, and as this occurs within the first 24 hours, exposure to the air is the most efficient treatment, as it dries the cementing substance. Laplace also obtains good results from the open method after grafting on healthy granulations. Bernhard grafts on healthy granulations and exposes the grafted area immediately to the sunshine. He says it dries and is stimulated and heals best by this treatment. On the other hand, Weischer and others claim that the results with the open method are not satisfactory.

FIG. 20.—Cage over the chest allowing exposure to the air of grafted area. The edges of the cage rest on a Bradford frame. Over the cage may be placed several thicknesses of gauze.

My own experience with grafts exposed to the open air has been quite satisfactory and this method is much facilitated by the use of moulded wire cages.

G. W. Davis suggests the use of wire shapes for the different parts of the body, having in the upper part a small flat tank covered with asbestos, and from this a flexible metal tube from which there is a constant drip of salt solution, to prevent the drying out of the grafts.

*Dressing of the Area from Which the Graft is Cut.*—All sorts of dressings have been tried, but the one finally adopted at the Johns Hopkins Hospital as the most satisfactory and comfortable is sterile boracic

acid ointment spread on sterile rubber protective. This dressing extends some distance beyond the margins of the wound, and is held in place by strips of adhesive plaster, and over this are put dry sterile gauze dressings and a bandage.

*Anesthetics.*—These grafts are as a rule cut under a general anesthetic, although several other methods have been suggested. Rose cites cases where he cuts grafts one to two inches wide, and as long as necessary, without the use of an anesthetic.

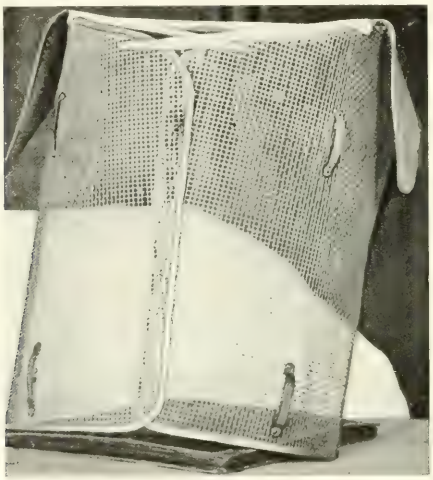

FIG. 21.—Front view of same cage, showing construction by the use of two ordinary wire splints.

Our experience has been that this can possibly be done in a limited number of cases, but not generally.

Torrance freezes the area to be cut with ethyl chloride, then cuts Thiersch grafts and transplants successfully.

Foot infiltrates small areas with salt solution, and then cuts from these areas.

In our series some grafts have been cut by freezing or cocainizing the external cutaneous nerve of the thigh, with little or no discomfort

to the patient, also by the use of ether spray over the field to be cut. Nystrom, in January, 1909, advises that whole-thickness and Thiersch grafts be cut after anesthetizing the external cutaneous nerve through the skin by means of 4 or 5 cc. of a 1 per cent solution of novocain, to which are added 5 drops of 1 to 1000 adrenalin solution to each 10 cc. This mixture is injected just to the inner side of the anterior superior iliac spine, then below it at various depths, in the subcutaneous tissues; some of the fluid being deposited under the fascia lata, but not too deeply into the muscles. It is an interesting fact that cocainization of the external cutaneous nerve of the thigh was first practiced at the

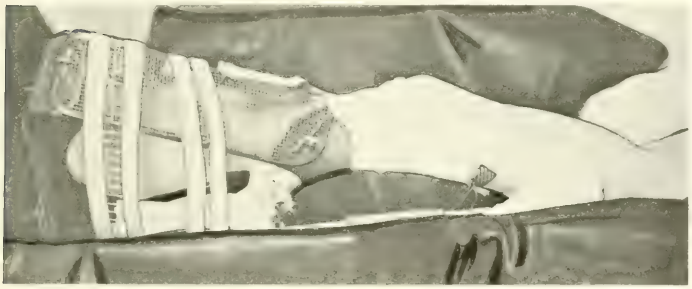

FIG. 22.—Wire cage for the exposure of a stump of the foot to the air, after grafting. This cage is made with a gutter for the support of the thigh and upper portion of the leg, the stump extending beyond the gutter. The snug bandage over the knee and around the cage extends the leg, and thus keeps the stump from touching the base of the cage. Note side and end braces.

Johns Hopkins Hospital over 15 years ago, for the purpose of cutting grafts, without pain, from the area supplied by this nerve, and this method is still occasionally used.

*Other Methods of Obtaining Thin Grafts.*—Kellock uses a combination graft cut in one piece. He marks out the square whole-thickness portion, then with a sharp razor cuts Thiersch grafts to the margins, and turns them back, then cuts the deep graft. This method is unnecessarily complicated, and leaves a defect to be filled.

Von Mangoldt's method is to scrape the skin with a razor, after it is carefully cleaned up. He discards the first scraping of the surface, but when the fine punctate bleeding of the tops of the papillæ is seen,

the layer with most vitality is reached. Then he scrapes thoroughly and transfers the mixture of blood and epithelial cells to the fresh wound and spreads it out evenly. This method is simple and convenient, and requires much less substance to cover extensive surfaces than do other technics.

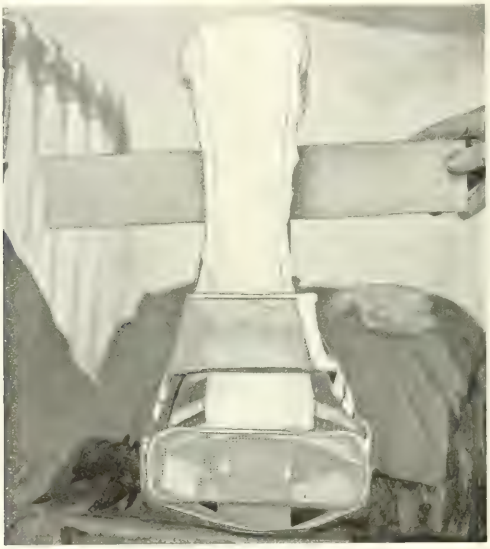

FIG. 23.—The same cage looking from above downward. The upper wire cross piece is hinged, and lifts up to allow placing the stump in the cage without danger of disturbing the grafts. The cross-board to be seen back of the gutter rests on the bed, and prevents the cage from tilting.

Noesske, in his paper on this method of grafting, claims that it has special advantages in lining cavities in long bones after operations for osteomyelitis. The cosmetic results are better than with the Thiersch method, but it requires a longer time for healing. It is best adapted to surfaces not exposed to friction.

*Lusk's Method.*—Lusk, in 1895, was impelled to try the use of dried shreds of epidermis over extensive burns, because no other skin was available, and secured such good results that he began to experiment.

The epidermis was obtained by vesication with a cantharides plaster, or from accidental burns and scalds. The fresh cuticle, after being cut off, was spread on gauze pads, or glass slides, and sterilized like any other surgical dressing. It was then thoroughly dried and kept until necessary. It should be applied dry, in small pieces, upon healthy granulating surfaces, not more than half an inch apart. He used gauze saturated in balsam of Peru, 1 drachm, and castor oil, 1 ounce, and the dressing was not changed for ten days or two weeks (Fig. 24).

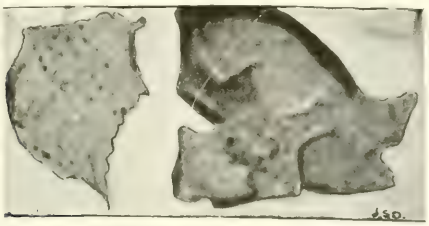

FIG. 24.—Two pieces of superficial epidermis, obtained by Lusk's method, which were spread out on a glass slide and sterilized.

Hodgin successfully transplanted dry epithelial scrapings, which were sown on the wound. Kibbler also was successful with thin sections of callus from the palms of the hands and soles of the feet.

### METHODS OF OBTAINING THICK GRAFTS.

*Living Whole-thickness Flaps.*—Before the technic of whole-thickness sessile flaps was perfected and proved so successful wherever a thick graft was necessary, better results were obtained by living pedunculated flaps with subsequent amputation of the pedicle. The ordinary transplantation from distant parts can be used in comparatively few cases, the forced position being very trying to the patient, and in addition a considerable defect is left. However, the area, as well as the raw surface of the flap, may be covered by Thiersch or whole-thickness grafts.

Many surgeons have reported methods, which bear their names, of transplanting such flaps, one or two of the most ingenious of which I will describe briefly.

Steinthal, in 1901, reported a double transfer of a whole-thickness flap for a nasal defect. He raised a rectangular flap from the thoracic or abdominal wall, and sutured the free end into an incision in the forearm, which was then immobilized.

After the circulation had become well established between the flap and forearm, the base pedicle was amputated. The arm, with the flap attached, was raised to the nasal defect, the flap secured and the arm immobilized. After a sufficient time, the base was amputated from the forearm. This allows somewhat more freedom in the selection of the flap, and is a valuable method. Finney, in 1908, used a similar method in the repair of a chin.

Hagen, in 1905, after freshening the wound, cut a whole-thickness pedunculated flap and bent it 180°, so that the raw surface was uppermost, and secured its rim to the edge of the defect, thus making a bridge, which was held up by a gauze pad. The defect from which the flap was lifted was grafted with immediate Thiersch grafts, and the entire wound dressed wet. After the circulation was established, the base of the flap was notched on both sides on the ninth day, and a few days later completely severed. Both the wound and subcutaneous tissue of the flap were then freshened and the flap applied to the defect.

Von Hacker, in 1888, described a similar method.

Finney (January, 1909) transplanted a whole-thickness living flap with a portion of the subcutaneous fat from one sister to another, using a large pedunculated flap from the right thigh of one to cover an extensive defect on the left foot of the other (the right leg of the grafted child having been amputated at some previous time above the knee). The parts were then immobilized in a plaster cast. It is of interest to note that Hamilton, in 1844, suggested a similar procedure for the relief of a traumatic ulcer of the leg, but was unable to carry it out.

In using living flaps, several points must be borne in mind. The form of the flap must correspond approximately to the form of the defect, and an allowance should be made of about a third more, for elastic shrinkage. Do not cut a flap with too pointed an extremity. Make the length of the flap conform as far as possible to the course of

the nutrient vessel. The subcutaneous fat must be of the same thickness throughout, if it is used. Never notch a pedicle in order to make it twist more easily into position, but prolong one of the side incisions. Pedicles of flaps to be twisted should be made narrower than the body of the flap, although never less than half the width of the flap. Sutures must be placed close to the skin edge in order to avoid any disturbance

FIG. 25.—The outline of a whole-thickness graft on the skin of the leg, which is 13.5 cm. long, by 4.5 cm. at its widest portion.

to the nutrition of the edges, and should never exert any tension. The pedicle may be amputated in from five to fourteen days, and the edges of the separated base should then be shaped and sutured into position.

Pedunculated flaps, which are properly cut, as a rule are successful. By this method the subcutaneous fat can be transplanted where desirable, as in Habhegger's case, although it seems unnecessary to transplant the fat, as we now know that it regenerates within a comparatively short time.

*Sessile Whole-thickness Flaps.*—Krause says that the three main things necessary for the successful transplantation of whole-thickness sessile flaps are total asepsis, perfectly dry technic, and suitable preparation of the area to be grafted. His method in detail is as follows:

*Preparation of the Part from Which the Flap is Taken.*—Bathe and shave. Sponge with ether, wash with sterile water and dry. Do not handle the skin in preparing it any more than is necessary.

FIG. 26.—The same area, with the skin and subcutaneous fat cut through, down to the deep fascia, leaving the flap intact on its bed. The flap now measures 9.5 x 3 cm. The size of the wound is 13 cm. long by 8.5 cm. wide. This plate shows the retraction of the skin edges and the contraction of the graft itself. This contraction varies slightly, according to the location from which the graft is cut

If the defect is not a fresh wound, excise the healthy granulating area, making it into a fresh wound; be sure that nothing wet touches the wound and use rigid aseptic technic. Check all hemorrhage completely (Figs. 25 and 26).

Mark out with a knife the flap to be cut in the shape of an elongated spindle, in order that the edges of the wound can be easily approximated, remembering that the skin immediately shrinks to about two-

thirds of its original size transversely, and a little less in its length. As an example of the shrinkage of a whole-thickness graft, the following measurements, taken from one of my cases, will be of interest: as marked out on the skin of the thigh before cutting, 14 x 3.75 cm.; after removal, 10 x 2.5 cm.; area of wound after removal of flap, 16 x 6.5 cm.

Flaps the whole length of the thigh may be taken in this way. Trim

FIG. 27.—Method of trimming off the subcutaneous fat from a whole-thickness graft. The flap rests on the fingers, the lower end lying on the palm of the hand, and the fat is rolled back as it is cut off in one piece with curved scissors.

off the subcutaneous fat as the flap is lifted, leaving it in its base, and put raw surface to raw surface, handling it as little as possible. In fat individuals it is necessary to excise subsequently the subcutaneous fat before closure is possible.

Apply the flap, after shaping with scissors if necessary, and press it down evenly with gauze, and it will adhere snugly, but this will not occur if any moisture has been introduced into the wound. Put a sterile gauze bandage immediately over the graft to hold it snug; then

dry gauze, bandage and splint. After four days remove the outside dressing and soak the limb in sterile boric solution, and open any blisters that may have formed, dress and keep in bed for at least three weeks. The superficial layers may be cast off. Krause says that this method is to be employed in all cases of extended defects in the skin of the limbs, where one used formerly the cutaneous pedunculated flap.

*Young's Method.*—Prepare the area from which the graft is to be taken, as for an aseptic operation. The surface to be grafted must be of firm fresh rose-pink granulations, smooth and level with the surface. Clean this area thoroughly on the day before the operation, without causing any bleeding, and put up in a mild wet antiseptic dressing.

Remove the flap, with all the underlying fat a third to a sixth larger than is required, by a few clean sweeps with a knife down to the fascia or aponeurosis covering the muscle. Place this in warm sterile normal salt solution, or 1/40 borax solution, until required.

Close and dress the fresh wound before the field to be grafted is exposed. Irrigate the granulating area thoroughly with normal salt or borax solution to remove any secretions, and dry with gauze, being careful to cause no bleeding.

Remove the flap from the solution, and lay it on the palm of the hand, raw side up, and rapidly trim off the fat with curved scissors (Fig. 27). Esmarch also removes the fat in this manner. Dry carefully with gauze, and apply it smoothly and evenly to the wound by firm pressure.

Cover the whole surface with book muslin impregnated with varnish, which will allow the free escape of any discharge. Then apply a warm normal salt or borax solution dressing, and cover the whole with rubber tissue. Dress daily down to the muslin. Young claims that by this technic not even the superficial layers are cast off, and the percentage of takes is very large.

Both of these methods are based on that of Wolfe, and are modifications and advances in the technic by which much larger whole-thickness pieces of skin may be successfully transplanted. The difference in the two methods may be summed up in a few words. Krause advocates a perfectly dry technic; separates the subcutaneous fat as he lifts the flap from its base, and only grafts on fresh wounds, or those made into fresh ones. He uses dry dressings. Young, on the other hand, uses wet

technic; cuts away the subcutaneous fat with scissors after excising the flap, grafts on undisturbed healthy granulations, and uses wet dressings.

Excellent results are reported by both methods, and both probably have their advantages in their respective fields. Young's method of obtaining the flap is quicker and more practical and can be used with either technic.

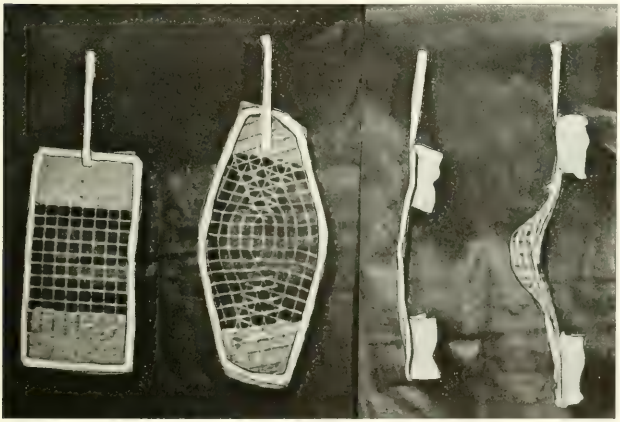

FIG. 28.—Small wire cages, front and lateral views. Similar cages can be moulded to fit almost any locality, and may be either very small or of considerable size. The whole cage, including the felt pads, may be wrapped up and sterilized with the other dressings.

I have had great success with whole-thickness sessile grafts by using the following technic: Obtain the flap by Young's method, and remove the subcutaneous fat, but use the dry technic throughout. Cleanse the granulations with normal salt solution without causing bleeding, and dry thoroughly. Then button-hole the flap here and there if it is a large one, or perforate freely with a saddler's punch and apply to the dry granulations, pressing it down snugly with gauze. Cover the flap with a rubber-impregnated splinting material, and dress with moist salt gauze, which is allowed to remain for 24 to 48 hours. Then re-

move the wet dressing, and allow the splinting material to remain in place. If possible expose to the air under a wire cage, after anointing the edges of the graft with a bland ointment (Figs. 28, 29 and 30). Otherwise dress with a very light dry gauze dressing held in place without much pressure. I use this same technic on Thiersch grafts, but remove the wet dressing within 12 hours. It is important to observe the grafts *every day,* in order to meet any unexpected complications that may arise during the healing.

FIG. 29.—Wire mesh cage on thigh, secured in place by adhesive straps.

The skin may be taken from almost any situation where there is sufficient laxity of tissue to admit of the suturing of the edges of the fresh wound.

In whole-thickness grafts it is best to choose the skin to be transplanted with some regard to the type of skin which will surround it. For instance, it is best, where transplantation to the face is proposed, to select the inner fore part of the upper arm, as it is thin and practically hairless. As the success of the flap depends on the blood supply of the mother soil, it follows that sessile flaps should not be placed on cartilage or be used for bridging over defects, but that pedunculated flaps be used for this purpose. However, sessile flaps can be success-

fully placed on healthy tendons, fascia, muscle, cortical and spongy bone, periosteum and even on the dura mater.

The ideal result desired in whole-thickness grafting is elasticity, softness, movability and normal color. All of these are obtained in a third of the full takes, although the same technic is used in all (Krause).

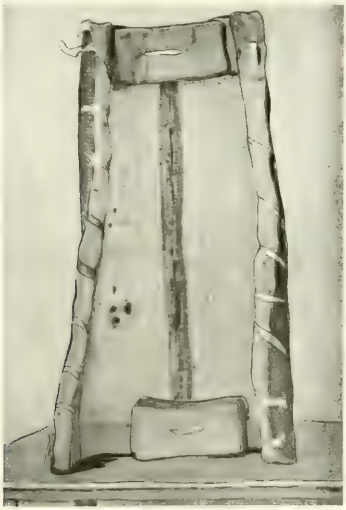

FIG. 30.—Same cage from below. Note felt pads where cage comes in contact with the thigh.

Krause mentions peculiarities sometimes shown in transplanted whole-thickness flaps. A brown pigmentation may appear which is in spots and stripes, and not evenly distributed. This probably originates from the broken down hemoglobin of the blood which remained in the flap, or from blood which entered from the substratum. The former can be guarded against by squeezing the flap gently between pieces of gauze before applying it. This discoloration is unimportant in the

covered portions of the body, but is much more serious on the face for cosmetic reasons. The flap may show a dark cyanotic color for months due to engorged venules. After a while the surface of the flap may become somewhat irregularly shriveled, which is probably due to the puckering of scar tissue in the depth of the wound. I have observed in several of my own cases the slight shriveling and the irregular pigmentation, and also the cyanosis due to enlarged venules, especially in those cases in which a considerable portion of the superficial layers sloughed.

While these changes in no way impair the efficacy of the flap, nevertheless they would prevent us, except in cases of necessity, from using sessile flaps on the face, plastics, pedunculated flaps and Thiersch grafts being best for this region.

Krause proved that there is a definite layer of adipose tissue under the transplanted flap three weeks after transplantation, and it is also a well-known fact that hair grows, and sweat glands regenerate in the flap, showing that the skin is transplanted with all that belongs to it. Whole-thickness grafts which are placed on untouched granulations project at first above the edges of the wound, but during the process of healing they assume the level of the surrounding skin.

The Thiersch method will of course remain the method of choice, on account of its simplicity and smaller operative action, but in such exposed localities as the elbow, palm of the hand, knee and heel, where there is considerable pressure and friction, these thin grafts will not stand the strain (Fig. 31).

*Preparation of the Granulating Area for Grafting.*—In order to put a granulating surface into the proper condition for grafting, various methods are employed. Among others may be mentioned, painting with tincture of iodine; touching frequently with nitrate of silver stick; dressing with balsam of Peru, either pure or in mixtures; with wet one to eight liquor sodæ chlorinatæ; wet boracic or salt solutions; two grains of chloral hydrate to the ounce of water, etc. I have found it very satisfactory after cauterizing thoroughly with pure carbolic acid to remove the granulations down to the firm base, then dress with dry gauze, over which is placed sterile boracic ointment, and it will be found that within 24 to 48 hours the new granulations will be flat, healthy and ready for grafting.

It is advisable to use large flaps, as the healing and adhesion is as good as with small ones, and there are fewer scars, and, therefore, less likelihood of future contraction.

It is seldom necessary to secure the flap in place. Extraordinary results have been obtained by the use of whole-thickness sessile flaps in most unfavorable cases, and this type of graft should be more gen-

FIG. 31.—The result of whole-thickness grafting on the palm of a contracted hand. Photograph taken 18 months after operation.

erally utilized. It is, of course, always wise to graft immediately a suitable defect in the skin following an operation, but should a granulating wound be presented the question arises as to whether it is best to graft on the untouched granulations, or whether the granulating wound should be made a fresh one by the removal of the granulations. My own observations have convinced me that both thin and whole-thickness grafts take just as well on an undisturbed granulating area as on a

fresh wound, provided that the granulations are clean, firm, rose-pink in color, and are not exuberant (Fig. 32).

The advantages of placing grafts on undisturbed granulations are that there is no pain during the preparation of the wound or application of the graft, and that less time is taken. There is also no loss of blood, or likelihood of blood or serum collecting under the grafts. There is no danger of stirring up infection. It is also said that the

FIG. 32.—Large ulcer on the outer side of the thigh, which is covered with flat, healthy granulations. Every graft placed on this wound was a complete take.

blood vessels enter the grafts much sooner if the granulations are not removed, this being proved by the fact that I have been able to obtain bleeding by cutting into a whole-thickness graft 84 hours after transplantation onto a healthy granulating surface, while the earliest record of bleeding in a similar graft on a fresh wound is 6 days, as noted by Krause. Furthermore, I have found that with this method isodermic grafts can be readily applied at the bedside, without having to carry the patient to the operating room, this being a great advantage in nervous cases.

Massage of the grafted area and surrounding skin is very advantageous, as it softens the graft, renders it more movable, and also causes it to assume more rapidly the appearance of the neighboring skin. This should not be started, however, for several weeks, until after the graft is firmly adherent to its base.

*Zoödermic grafting* has been tried for years with more or less success, grafts being taken from many species, among which may be mentioned, the inner surface of a pullet's wing, skin from pigeons, young puppies, guinea-pigs, rats and rabbits. Bartoux and Dubousquet-Laborderie successfully implanted the skin of frogs on a granulating surface in man. The pigment disappeared in 10 days, and the grafts rapidly changed character, resembling more and more the human skin. Cannaday grafted with fair success the skin of a common water lizard.

Sponge grafting was brought out by Hamilton, of Edinburgh. The granulating wound was accurately covered with thin sections of a fine sponge, previously prepared, and these sections were replaced as the granulations grew. The wound was dressed with protective and 1/20 wet carbolic gauze. Healing was very slow. This method was soon abandoned.

Bits of muscle have been applied to granulating wounds, and more rapid epidermization was claimed. The lining membrane of a hen's egg, cut in strips and applied with the shell surface uppermost, has also been used. Riven, and also Browning, successfully transplanted the superficial layers of the skin of a young pig, and it was noted that the pigment rapidly disappeared. Flegenheimer transplanted whole-thickness flaps with good results from the belly of a young pig, and states that fine hair grew on the graft.

Miles transplanted the skin of dogs, rabbits, kittens and frogs. He was most successful with grafts from dogs, and least successful with frog skin. A young animal was always selected. It was killed, and after cleansing thoroughly the skin of the abdomen, whole-thickness flaps without the subcutaneous fat were removed. These were placed in sterile boric solution, trimmed to fit the wound and pressed in on healthy undisturbed granulations. He quotes four successful cases, and notes that the pigment rapidly disappears, and that no hair, sweat or sebaceous matter can be found in the skin.

During the last few months I have taken whole-thickness grafts without the subcutaneous fat from the abdomen of young fox terriers,

and transplanted them on patients with ulcers following burns, and found that in most cases they would take, but that they macerated very easily, especially when dressed with any ointment. So I now follow the technic described under whole-thickness grafts with better lasting results. The pigment in these grafts rapidly disappeared. It is also an interesting fact that human skin can be successfully transplanted to an animal. Figs. 33 and 34 show a whole-thickness 50-hour graft 3 x 8 cm. from a negro which has taken perfectly on a prepared

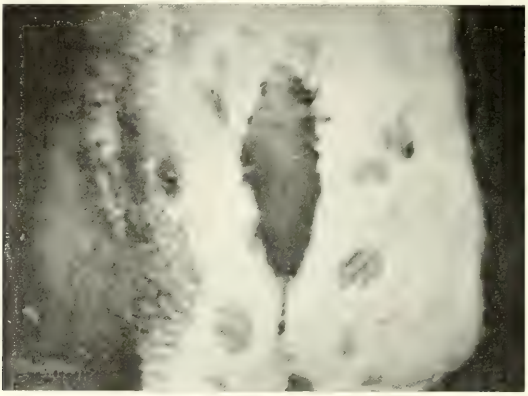

FIG. 33.—Whole-thickness graft from a negro, which has taken on the abdominal skin of a dog.

defect in the white abdominal skin of a four-months-old dog. In this case not even the superficial layers have been cast off, and the skin is soft and looks and feels as it did before applying it.

The photograph was taken on the eighth day, but further observations were prevented, as a few hours later the dog had to be killed on account of distemper.

Loeb and Addison, in a series of experiments on the transplantation of guinea-pig skin into animals of different species, came to the conclusion that there was a distinct connection between the condition of the growth of the transplanted skin and the relationship between the

guinea-pig and the animal into which the skin had been transplanted, and suggest as a cause the presence of toxic substances in the organisms of a different species.

*Another method of hastening epithelization* may well be considered at this time. V. Schmieden has been using 8 per cent Scarlet R salve to promote the healing of large skin defects, and finds that an ex-

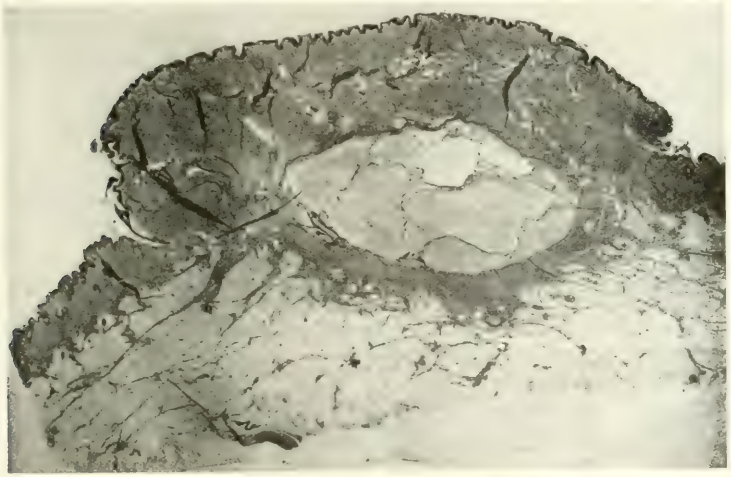

Fig. 34.—Microphotograph of section through the graft, shown in Fig. 33. At each end of the section can be seen an area of normal dog skin, with hair follicles, etc. Between these two areas is situated the whole-thickness graft, which is nearly normal in appearance. Under the center of the graft a collection of serum has formed, which is surrounded by a wall of fibrin, and through this are bands of fibrin. This collection of serum could have been avoided had the graft been button-holed. In the fat below the serum there is a layer of granulation tissue, extending in both directions to the wound edges and the graft. With high power many vessels from this layer can be seen penetrating the graft. (Microphotograph by Schapiro.)

tremely vigorous and thick epithelium, starting from the edges, rapidly covers the wound. The epithelium thus grown seems normal in every respect, and promises to shrivel less than under other conditions. The granulations must be as clean and healthy before applying the salve

as those required for Thiersch grafts. It has a marked irritating action, and at first the granulations turn grey and sometimes suppurate. He never applies the salve for longer than 24 hours, following it with plain lanolin or oil dressings for several days until all signs of irritation have passed off. He does not think there is any danger of cancer in this proliferation of epithelium. He says the effect is evidently a chemotactic action specific for epithelial cells.

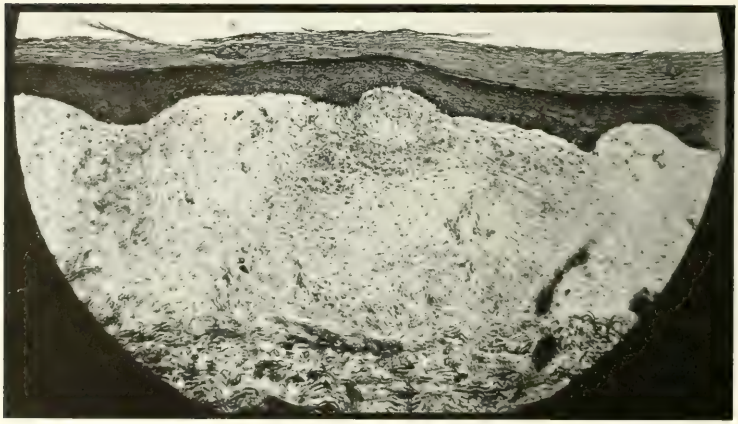

FIG. 35.—Section of the area from which a Thiersch graft was cut. The stratum corneum and stratum Malpighii are seen to be somewhat thinner than in normal skin. Papillary formation is practically lacking. There is a scanty amount of granular pigment in the deeper layers of the stratum Malpighii. Beneath the epidermis is the corneum, with connective tissue cells in various stages, leucocytes and red blood corpuscles. (Microphotograph by Schapiro.)

Kaehler also advocates this dressing. Krajca is enthusiastic on the results of the treatment with Scarlet R ointment. He has used it in connection with partial Thiersch grafting on a large granulating area, and reports great rapidity of healing. My own experience with Scarlet R in the Johns Hopkins Hospital Out-Patient Department has convinced me that in many cases its stimulation of the epithelium edges is quite remarkable. The results of this method of treatment were

reported in the June number of the Johns Hopkins Hospital Bulletin, 1909. In September of the same year, Hayward, after experimenting with the component parts of Scarlet R, came to the conclusion that the stimulating property was due to amidoazotoluol. My own observations on the efficacy of this treatment will be reported more fully later.

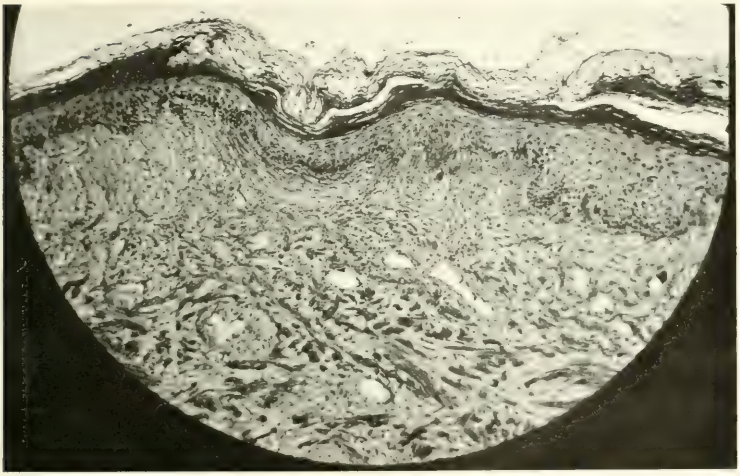

FIG. 36.—Section of the grafted skin with the stratum corneum partly detached. The variation in the thickness of the stratum Malpighii is probably due to the uneven cutting of the graft. There are many pigment granules in the deeper cells of the stratum Malpighii, while in places the pigment is scattered throughout this layer. Beginning papillary formation can be seen. (Microphotograph by Schapiro.)

*Histological Changes.*—The histological changes in the healing process of skin grafts are, in general, similar to those which take place in the healing of an ordinary clean wound. There is an exudation of fibrin between the graft and the wound upon which it is placed, which fixes the graft firmly. This fibrin layer is infiltrated by leucocytes and fibroblasts, and vascular sprouts soon begin to form and penetrate any portion of the corium which may have been transplanted, so that within a comparatively short time the graft is supplied with blood. These

vessels have been demonstrated by injection in epidermic grafts on the second day, and in cutis grafts on the third day (Enderlen). As early as the sixth day, a whole-thickness sessile flap, on a fresh wound, will bleed when cut (Krause), and I have obtained bleeding in 84 hours in a whole-thickness graft, placed on healthy granulations. In thin

FIG. 37.—The skin edge thrown into folds by the pursestring suture with the graft joining it. There are no pigment granules in this portion of the graft, and practically none in the skin immediately adjacent. (Microphotograph by Schapiro.)

grafts the upper layers macerate, leaving the deeper layers intact. In whole-thickness grafts there may be practically no maceration whatever, or the lower layers of the corium may alone remain viable, and the cells of the ducts of the sweat glands and hair follicles in this layer, which degenerate after transplantation, soon regenerate. These changes, however, do not interfere with the efficacy of the grafts. The graft itself takes an active part in the healing process after the third

or fourth day, there being a marked proliferation of cells into the underlying exudate, and an outgrowth of new epithelial cells spreading in all directions from the edges of the graft (Figs. 35, 36 and 37).

Enderlen says the fibrous and elastic tissues of the grafts gradually degenerate, and are replaced by newly formed tissue, which probably develops, at least in part, from the pre-existing elements of the graft itself, as well as from old fibers in the neighboring deeper tissues. In about two weeks the underlying granulation tissue is replaced by connective tissue, and this is finally the true cicatrix. The papillary structure of the newly formed skin is said to be well marked in three to four months, although in Fig. 36 we can see the beginning of the papillary structure, two weeks after grafting. A thin layer of adipose tissue was found by Krause, after three weeks, under a whole-thickness transplanted flap denuded of fat, and I have been able to demonstrate fat on a similar flap, placed on undisturbed granulations, on the fifteenth day after transplantation. This is most important, as it prevents, to a large extent, future contraction, and insures movability. The scar tissue beneath the transplanted skin continues to grow for several months. The union of the transplanted skin requires some time, and this fact must be borne in mind in order that the newly covered area be not exposed too soon to irritation and trauma. Within five weeks sensation begins to be restored to the transplanted skin, which regains tactile sensibility first, then pain and temperature sense. Although Stransky says that the nerve fibers enter from beneath and join the end organs in the flap, it is very much more likely that Wagner's idea, that nerve fibers grow in from the periphery, and not from the substratum, is correct, this being shown by the border sections always regaining sensation first. If the flap is large the central portion may for a long time remain anesthetic, while both thin and thick grafts may remain less sensitive throughout for years. I have noted this phenomenon in practically all of my own cases (Fig. 38).

*Changes in Pigmentation.*—The changes occurring in the pigmentation of transplanted skin are interesting. It is to be noted that in negro skin the pigment lies almost entirely in the deeper cells of the stratum Malpighii, and is practically lacking in the superficial cells. Reverdin established the fact that a pigmented thin graft from a negro transplanted upon white skin gradually fades, and this has been

confirmed by many observers, and also by the experience at the Johns Hopkins Hospital.

FIG. 38.—Stump of the upper third of leg, which was grafted completely 14 years ago. The outline of the grafted area can be seen; the grafted skin is markedly pigmented and is thrown in folds in places, due to pressure from the artificial leg. There is shriveling of the skin, which is still quite adherent to the underlying tissues. On the end of the stump is an ulcer, caused by accidentally dipping it into boiling water, which fact was not recognized at once, there being complete anesthesia of the grafted area, except for about ½ inch from the normal skin, as shown by dotted line (Bloodgood's case). (Photograph by Schapiro.)

However, Pollock mentions a case where a superficial graft remained colored. Maxwell reports a case in which he transplanted a small superficial graft from his own skin in addition to some black grafts on

a defect on a negro's face, and states that the white graft remained white. Two cases are reported by J. H. W. Mayer, in which negro skin was grafted on white patients, and he says that in both instances the grafts remained black. He does not mention the kind of graft used. T. Bryant also reports a case in which several small black grafts,

FIG. 39.—Returning pigmentation in lines and patches in ulcers healed by the use of Scarlet Red ointment. The isolated spots of pigment, entirely separated by unpigmented skin from the pigmented edges, are to be noted. The return of pigmentation in grafts is somewhat similar to this.

after transplantation to a white man, spread and joined each other, and finally made one black patch, which remained black (Fig. 39).

Karg says that a white graft placed on a negro after six weeks became dusky, and from the edges black stripes extended into the white skin, and black points or spots appeared in other places. The pigment gradually increased and in ten weeks the color was as black as the

surrounding skin, although the contour of the transplanted piece was still distinct. In another case of a black Thiersch graft on white skin he found after two weeks that the edges of the graft were lighter, then the central portion faded, and in about five weeks this also became a pale grey. The microscopic examination of the white skin grafted on the negro showed that after four weeks the epidermis in the center was entirely free of pigment. Numerous ramified pigment cells were found in the periphery, on the boundary line between the cutis and epidermis, which sent fine offshoots between the cells of the epidermis. Granular pigment was found here and there in the epidermic cells, especially near the ramified pigment cells. Pigment granules were also found in the upper layers of the cutis, particularly in the neighborhood of the vessels. All of these were much increased, after eight weeks, and after twelve weeks the pigmentation was so intense that the offshoots of the pigment cells could not be made out. From these observations Karg concludes that the pigment is brought to the colorless epidermic cells by cells of a connective tissue nature derived from the cutis, and that they represent special chromatophores.

The black skin grafted on the white was within six weeks entirely free of pigment, except single pigment granules in the corneal layer, and larger flakes in the cutis. Single cells containing pigment were also found deeper down. The pigment, therefore, seems to be taken up and removed by migratory cells. The ramified cells with offshoots can be seen between the epidermic cells, but contain no pigment. It is interesting to note that when a whole-thickness black graft is placed on a black patient, the layers containing the pigment are cast off, the graft is left perfectly white and the pigment slowly returns in the course of time.

Leo Loeb experimented by transplanting the pigmented skin of a guinea-pig to a place where the skin is unpigmented, or conversely. He says that following the transplantation, the black skin not only keeps its own pigment, but after a variable period the boundaries of the transplanted skin, which before were very distinct, become indistinct, a darker line appearing at the margins, and gradually the pigmented area spreads in the white skin. The same thing happens under certain conditions where white skin is transplanted to dark, the black pigment spreading in the white skin. He thinks the living white

epithelium is replaced by the transplanted black epithelium by a process of infiltration, and that under these circumstances there are no signs of phagocytosis, by which the black cells destroy the white ones, and further that the chromatophores originate from the epithelium itself, and at no time are migratory from deeper tissues.

Karg and Loeb both worked along similar lines, but Karg used Thiersch grafts on human beings, while Loeb experimented with whole-thickness grafts on guinea-pigs. The findings of Karg are generally accepted, and seem the most reasonable.

I have been able to transplant several white whole-thickness grafts onto negroes, and found that after a considerable time they became dusky, the duskiness starting especially on the portion of the graft nearest the normal skin. On those grafts, which were placed at some distance from the skin edge, pigmentation occurred considerably later, as it was apparently necessary for the intervening space to become pigmented before the graft took on its pigment. In the cases where negro whole-thickness grafts have been placed on white skin, the pigment layer is soon cast off, and as yet I have seen no return of the pigment.

*Persistence of Vitality of Grafts.*—Martin, in his series of experiments, found that none of his grafts lived and were effective after 108 hours in "free air" at a temperature of nearly zero Centigrade = 32° Fahrenheit, but that when kept in hermetically-sealed tubes, or "confined air," under the same temperature conditions, the grafts could be successfully transplanted. Under similar temperature conditions another graft was successful, after 96 hours in "free air." Where the temperature was 6° Centigrade = 42.8° Fahrenheit, the limits were 82 hours in "free air" and 96 hours in "confined air." At 12° Centigrade = 53.6° Fahrenheit, the limits were, 72 hours in "free air" and 84 hours in "confined air."

At 15° Centigrade = 59° Fahrenheit, the limits were, 60 hours in "free air" and 72 hours in "confined air."

At 20° Centigrade = 68° Fahrenheit, the limits were, 36 hours in "free air" and 36 hours in "confined air."

At 28° Centigrade = 82.4° Fahrenheit, the limits were, 6 hours in "free air" and 7 hours in "confined air," respectively.

He came to the conclusion that cold favored the success of trans-

plantation, and heat was unfavorable and caused shorter duration of vitality. Also that moisture hastened decomposition, smaller masses lived the longer and grafts were best preserved in hermetically-sealed tubes at low temperature. It must be remembered that these experiments were made before the days of asepsis.

FIG. 40.—An ulcer of the outer aspect of leg, on which may be seen a 14-hour whole-thickness graft 11 x 12.5 cm. and a smaller 64-hour whole-thickness graft 4 x 3 cm.

Brewer was able to use successfully Reverdin grafts obtained from skin removed from the body as long as 36 hours, but not longer.

The skin of amputated limbs has also been successfully transplanted from 36 to 96 hours after amputation. I have successfully transplanted onto healthy undisturbed granulations pieces of whole-thickness skin, taken from a leg 18 hours after amputation, at various intervals, up to 30 days. The superficial portions of the grafts kept over 48

hours sloughed, and only the bases adhered. Some of the grafts were several centimeters in diameter. This skin was kept in an ordinary ice chest in a sterile jar plugged with cotton, containing a moist normal salt gauze sponge. I have observed that whole-thickness grafts which are to be preserved for any length of time will take better if the subcutaneous fat is allowed to remain intact until the time the graft is needed (Figs. 40 and 41).

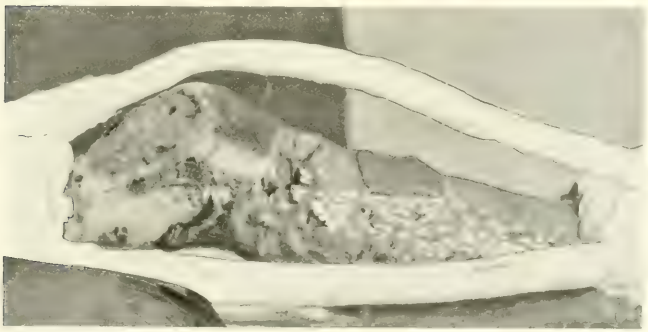

FIG. 41.—Ulcer following burn of leg. The leg is in a plaster of Paris cage. This cage allows exposure to the air, and also holds the limb extended in those cases where contraction is feared. Two whole-thickness grafts can be seen on the upper third of the shin. A piece of wire netting, placed around this framework and secured to it, is sometimes advantageous.

Girdner successfully grafted skin from a cadaver 6 hours after death. Many others have also obtained grafts in this way.

Ljungren grafted successfully pieces of skin kept in sterile ascitic fluid from two days to three months, and the microscope showed that the epithelium had multiplied by karyokinesis.

Wentscher was able to graft successfully pieces of skin kept from seven to fourteen days in sterile tubes with moist salt gauze and cotton plug, and was able to demonstrate mitosis. He concluded that grafts can be used with safety from 24 to 48 hours after cutting, but as a rule not longer than 48 hours.

Burkhart found that grafts lost nothing in vitality if applied 24

hours after being cut, either on fresh wounds or untouched granulations. This has also been my experience, especially with whole-thickness grafts. He obtained partial success with grafts preserved eight days in a moist chamber, and twelve days in a dry chamber. In cases where there was much bleeding he applied the grafts 24 hours later, after all hemorrhage had ceased.

Dried epidermic scales have been successfully transplanted 418 days after removal from the patient.

*Transplantation of Mucous Membranes.*—The transplantation of mucous membranes on men and animals has been tried for many years with little success. In 1871 Czerny successfully transplanted small pieces of mucous membrane from the uvula upon two breast cancer wounds. Ciliated epithelium from a nasal polypus applied to granulating areas was successful in two out of three cases. These caused a skinning over of the wound with flat tender epithelium which was gradually displaced by epidermic cells.

FIG. 42.—Israelson's double knife for the transplantation of mucous membranes.

This procedure is used principally in conjunctival defects, and the membrane is obtained preferably from the lips and cheeks.

On several occasions I have been able to transplant successfully good-sized pieces of vaginal mucosa on healthy granulating areas.

Wolfler, Bock, Djatschenko and Raehlman have also experimented with more or less success along this line. The only case at the Johns Hopkins Hospital was that in which the mucous membrane from the cheek of a dog was grafted on a defect in the cheek of a boy. The result was a total failure (Fig. 42).

Following the suggestion of Mr. W. L. Thornton, of the fourth year class, I have tried grafting pieces of the lining of the amniotic sac, but as yet am unable to report favorable results. The material is well worth a trial, and if a technic is developed by which favorable results can be obtained, it may be of great use.

In the 550 cases reported here, the large majority have been those

in which it seemed best to use thin grafts, this being especially called for in covering the defect in the skin left by a complete breast operation. Most of the grafts were obtained by the modified Thiersch method, as described above; a few by Reverdin's epidermic method, and one or two by Lusk's blister method. Comparatively few thick grafts have been used, only twenty-three cases in all, thirteen being whole-thickness sessile flaps, and ten whole-thickness pedunculated living flaps, from distant parts. Sliding plastic flaps from the adjacent skin were used when possible, and the defect immediately covered with a Thiersch graft. A number of cases have been grafted in the Out-Patient Department whose records I have been unable to obtain.

The ulcers following breast operations were allowed to heal by granulation until July 6, 1896, when one was grafted for the first time by Dr. Bloodgood. On October 5, of the same year, a partial immediate graft was tried at the time of the operation, also by Dr. Bloodgood, and since that time practically every defect following a breast operation, in which the skin edges could not be approximated, has been grafted with a complete immediate graft.

The graft was first spread on protective on March 7, 1896, which procedure greatly facilitates placing it in position. The attempt is always made to cover the defect with a single graft, consequently very large single grafts have been cut. The notes on the measurements of both grafts and defects to be covered are very incomplete, but the following may be mentioned: 8 x 10 cm., 8 x 12 cm., 8 x 16 cm., 10 x 18 cm., 12 x 12 cm., 16 x 16 cm. and 15 x 16 x 14 cm. (irregular shape). These measurements were taken after cutting on breast cases. Size of defect to be covered: 8 x 10 cm., 10 x 10 cm., 10 x 12 cm., 11 x 11 cm., 12 x 12 cm., 12 x 14 cm., 14 x 14 cm., 15 x 15 cm., 20 x 20 cm. and 19 x 23 cm. Results show that these larger grafts take as well as the smaller ones.

Thin Thiersch grafts of uniform thickness take better than those of varying thickness. Large grafts cannot be cut from a fat or flabby thigh.

Several contractions have recurred under Thiersch grafts, especially those placed on the palm of the hand, and there seems to be no doubt but that a whole-thickness graft in this and other exposed locations would be more satisfactory.

Several cases of phlebitis of the long saphenous vein followed cutting grafts from the left thigh, and for this reason the right thigh is used whenever practicable, no case of phlebitis having yet followed cutting on this side.

In quite a number of cases black Thiersch grafts have been placed on white patients, and white grafts on black patients, with fair results. The pigment disappears, or appears, after a comparatively short time in the Thiersch grafts, but there is no case in our series which will show the effect of the pigmentation of a whole-thickness graft thus transplanted.

When more skin than was required was cut, in several cases it was grafted on the wound from which it came with complete success.

What seems to be a failure at the first dressing will sometimes turn out very well, and vice versa. Some grafts are moist and there is considerable secretion throughout the healing process, while others are perfectly dry. In the moist variety a strong characteristic glue-like odor is often noticed. This moisture is probably due to secretions, which are held back by the silver foil and paper, which becomes saturated soon after the operation and then dries and forms an impermeable dressing, preventing the further escape of the secretions and also the ingress of air. Any one who has dressed grafted wounds covered with silver foil and paper will have noticed this fact in many cases, while in others the secretions do pass through and leave the wound dry. This latter group is especially noticeable in those instances where alcohol is not used to moisten the paper in order to make it adhere more closely. In fact if the paper is used at all on these cases, which is unnecessary, it should not be moistened with the alcohol, both for the reason mentioned above, and also because the alcohol is injurious if it soaks through to the graft. It is best, therefore, to omit the paper and alcohol and to place dry gauze immediately next to the foil.

Too much pressure of the dressing on the grafted area may cause sloughing of the freshly-applied graft, and a heavy dressing, causing too much heat and sweating, is to be avoided. In the majority of cases, the wound caused by the cutting of the graft is healed some time before the patient is ready to leave the hospital.

In this series I have counted as a single case all the grafting done on any one patient during his particular hospital admission. For

instance if the patient is grafted at two different times, or has two defects grafted at the same time, both being completely successful, this is called one complete take.

Should one graft completely take and the other partially take, then this would go under complete and partial takes, etc.

Only those cases have been tabulated in which there was not a complete take, while the complete takes have been simply summarized.

PARTIAL TAKES. CLEAN CASES

| SEX AND AGE. | FOR RELIEF OF. | KIND OF GRAFT. | DRESSING. | REMARKS. |
|---|---|---|---|---|
| F. 37 | Defect following operation for carcinoma of breast. | Immediate autodermic Thiersch. | Silver foil. | Wound 5 x 8 cm. No slough of axillary flap. Almost complete take. Discharged with 2 small granulating areas. |
| F. 47. | Do. | Do. | Do. | Almost complete take. No slough of axillary flap. Practically healed when discharged. |
| F. 35. | Do. | Do. | Do. | Wound 8 x 9 cm. Complete take, except area 1 cm. in diameter. No slough of axillary flap. Discharged with small granulating area. |
| F. 26. | Do. | Do. | Do. | Slight wound infection. Grafts $\frac{4}{5}$ take. Slough of tip of axillary flap. Healed when discharged. |
| F. 40. | Do. | Do. | Do. | Almost complete take. No slough of axillary flap. Healed when discharged. |
| F. 46. | Do. | Do. | Do. | Wound 10 x 15 cm. Almost complete take. No slough of axillary flap. 1 or 2 small granulating areas which were closing rapidly when discharged 18 days after operation. |
| F. 39. | Do. | Do. | Do. | Wound 6 x 12 cm. Almost complete take. Small slough in center of graft. No slough of axillary flap. Closing rapidly when discharged 15 days after operation. |
| F. 45. | Do. | Do. | Do. | Complete take except on edges. No slough of axillary flap. Almost healed when discharged. |
| F. 39. | Do. | Do. | Do. | Take of major portion of graft. Superficial epithelium sloughed. No slough of axillary flap. Discharged with small granulating area. |
| F. 43. | Do. | Do. | Do. | Entire graft sloughed with the exception of a few islands. No slough of axillary flap. No wound infection. No cause made out for large amount of slough except possibly too much pressure, as patient complained of tightness of dressing. Discharged with granulating area. |
| F. 44. | Do. | Do. | Do. | Take except along edges. Some slough of tip of axillary flap. Patient collapsed |

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| | | | | | healed when discharged. |
| F. 48 | Do | Do | Do | | One-half take. Slough of part of axillary flap. Discharged with small granulating area. |
| F. 55 | Do | Do | Do | | Grafted wound 2 cm. deep. Almost complete take. Slight slough of axillary flap. Discharged with 1 small granulating area. |
| F. 65 | Do | Do | Do | | Almost complete take. Slough of tip of axillary flap. Discharged with small granulating area. |
| F. 40 | Do | Do | Do | | Almost complete take. Slough of part of axillary flap. Discharged with small granulating area. |
| F. 35 | Do | Do | Do | | Wound 11 x 11 cm. Slough 2 cm. in diameter, in center of graft. No slough of axillary flap. Discharged with small granulating area. |
| F. 50 | Do | Do | Do | | Almost complete take. No slough of axillary flap. Discharged with small granulating area. |
| F. 64 | Do | Do | Do | | Same as above. |
| F. 62 | Do | Do | Do | | Two-thirds take. Slough of axillary flap. Discharged with small granulating area. |
| F. 46 | Do | Do | Do | | Wound 7 x 10 cm. Take of greater portion of graft. No slough of axillary flap. Discharged with small granulating area. |
| F. 48 | Do | Do | Do | | Almost complete take. Few small granulating areas. No slough of axillary flap. No discharge note. |
| F. 59 | Do | Do | Do | | Four-fifths take. No slough of axillary flap. Healed when discharged. |
| F. 62 | Do | Do | Do | | Two-thirds take. Marked slough of axillary flap. Healed when discharged. |
| F. 29 | Do | Do | Do | | More than $\frac{3}{4}$ take. No slough of axillary flap. Discharged with small granulating area. |
| F. 37 | Do | Do | Do | | Wound 9 x 12 cm. Almost complete take. No slough of axillary flap. Healed when discharged. |

PARTIAL TAKES. CLEAN CASES. Continued.

| SEX AND AGE. | FOR BUILT-UP | KIND OF GRAFT. | DRESSING. | REMARKS. |
|---|---|---|---|---|
| F. 56 | Defect following operation for carcinoma of breast. | Immediate autodermic Thiersch. | Silver foil. | Complete take, except around edges. No slough of axillary flap. Case hopeless. Left hospital against advice with small granulating area. |
| F. 43 | Do. | Do. | Do. | Nine-tenths take. Slough of tip of axillary flap. Healed when discharged. |
| F. 37 | Do. | Do. | Do. | Wound 12 x 12 cm. ½ take. Considerable discharge from wound. No slough of axillary flap. No discharge note. |
| F. 28 | Do. | Do. | Do. | Three-fourths take. No slough of axillary flap. No discharge note. |
| F. 29 | Do. | Do. | Do. | Wound 12 x 12 cm. Some of graft slipped. No slough of axillary flap. Discharged with 2 small granulating areas. Returned 2 years later with metastases in the dura. Grafted area measured 13 x 15 cm. Skin firmly adherent to ribs except at margin. |
| F. 64 | Do. | Do. | Do. | Wound 15 x 15 cm. Complete take except small area in center of graft. No slough of axillary flap. Healed 26 days after operation. |
| F. 49. | Do. | Do. | Do. | Wound 12 x 12 cm. About ½ take. Slough of tip of axillary flap. Closing rapidly when discharged. |
| F. 64. | Do. | Do. | Do. | Slight slough along edges of graft. No slough of axillary flap. Practically healed when discharged. |
| F. 37 | Do. | Do. | Do. | Take of nearly all of grafts. Several small granulating areas. No slough of axillary flap. Healed when discharged. Seen 1 year later. Grafted area measured 10 x 15 cm. Adherent to ribs, except in lower part. |
| F. 39 | Do. | Do. | Do. | Almost complete take. No slough of axillary flap. Practically healed 21 days after operation. |
| F. 63 | Do. | Do. | Do. | One-half take. Blood clot under the other half. No slough of axillary flap. Entirely healed when discharged, 5 weeks later. |

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|---|---|---|---|---|---|
| | | | | | Two-thirds take. No slough of axillary flap. Discharged with granulating area 1 month later. |
| | | | | | Almost complete take. Few small sloughs in center of graft. No slough of axillary flap. [illegible] discharged 3 weeks later. |
| | | | | | Complete take except [illegible] cm. No slough of axillary flap. [illegible] discharged 23 days after operation. |
| | | | | | Almost complete take. No slough of axillary flap. Discharged with [illegible] granulating areas. |
| | | | | | Wound 12 x 12 cm. Almost complete take. No slough of axillary flap. Plaster on opposite side followed operation. Healed when discharged. |
| | | | | | Almost complete take. No slough of axillary flap. Many islands of buried tissue after operation. Discharged with [illegible] granulating areas. |
| | | | | | Wound 10 x 12 cm. Almost complete take. Slough of tip of [illegible] flap. Healed when discharged. Wound then measured 7 x 11 cm. |
| | | | | | Almost complete take. No slough of axillary flap. [illegible] operation. Discharged with granulating areas. |
| | | | | | Wound very large. Almost complete take. No slough of axillary flap. Plaster on opposite side followed operation. Discharged with [illegible] granulating areas. |
| | | | | | Complete take, except [illegible] No slough of axillary flap. Discharged with [illegible] area 16 days after operation. |
| | | | | | Wound 8 x 12 cm. Complete take except at [illegible] No slough of axillary flap. Healed [illegible] operation. |

PARTIAL TAKES—CLEAN CASES—Continued

| SEX AND AGE | FOR RELIEF OF | KIND OF GRAFT | DRESSING | REMARKS |
|---|---|---|---|---|
| F. 18 | Defect following operation for carcinoma of breast. | Immediate autodermic Thiersch. | Silver foil. | Almost complete take, except area ½-3 cm. No slough of axillary flap. Nearly healed when discharged. |
| F. 47 | Do | Do | Do | Wound infected. Take of only few islands. No slough of axillary flap. Discharged with large granulating area. |
| F. 56 | Do | Do | Do | Almost complete take. No slough of axillary flap. Irregular-shaped wound, 10 x 12½ x 0.5 cm. 29 days later wound measured 9 x 10½ x 0 cm. Healed when discharged. |
| F. 47 | Do | Do | Do | One-third take. Wound infected. No slough of axillary flap. Discharged with granulating area. |
| F. 42 | Do | Do | Do | Almost complete take. No slough of axillary flap. Few small granulating areas when transferred to medical side. |
| F. 68 | Do | Do | Do | One-half take. Remainder slipped. Slough of tip of axillary flap. Healed when discharged. |
| F. 45 | Do | Do | Do | Almost complete take. No slough of axillary flap. Healed when discharged. |
| F. 41 | Do | Do | Do | Nine-tenths take. No slough of axillary flap. Healed when discharged. |
| F. 70 | Do | Do | Do | Nine-tenths take. Wound infected. Slough of tip of axillary flap. Discharged with small granulating area. |
| F. 50 | Do | Do | Do | One-half take. Slough of tip of axillary flap. Wound looked unhealthy. Discharged with granulating area. |
| F. 41 | Do | Do | Do | Almost complete take. Recurrence in scar. Healed when discharged. |
| F. 68 | Do | Do | Do | One-half take. Over ½ of graft slipped. Slough of tip of axillary flap. Discharged with small granulating area. |
| F. 44 | Do | Do | Do | Almost complete take. Slough of tip of |

| | | | | | |
|---|---|---|---|---|---|
| [illegible] | Do | Do | Do | Almost complete take. No slough of axillary flap. Many varieties of graft. Discharged with few small granulating areas. |
| [illegible] | Do | Do | Do | Almost complete take. No slough of axillary flap. Slight rise of temperature during the first few days after operation. Discharged with small granulating area. |
| [illegible] | Do | Do | Do | Almost complete take. No slough of axillary flap. Graft at first dressing looked like complete take, but several small sloughs appeared later. Discharged with small granulating area. |
| [illegible] | Do | Do | Do | Almost complete take. No slough of axillary flap. Patient's general condition very poor. Dry tube in long. Evening rise of temperature. Discharged with small granulating area. |
| [illegible] | Do | First and second grafting unsuccessful. Third successful. | Do | First grafting, ½ take. Slight slough of axillary flap. Thrombosis of median basilic vein, corrected. Pharynx on opposite side. Second grafting, about graft, ½ take. Nearly healed when discharged. |
| [illegible] | Do | First grafting unsuccessful. Second grafting successful. Third failed. | Do | Wound 1 x 1 cm. Grafting. Failure. Staphylococcus aureus. Second graft. No slough of axillary flap. Uncovered area regarded. Another graft clipped. Take at remainder. Discharged with small granulating area. |
| [illegible] | Ulcer of breast. Excision. Complete operation. Sutures. | Unsuccessful. Third successful. | Do | Wound 3½ x 2½ cm. Almost complete take. No slough of axillary flap. Nearly healed when discharged. |
| [illegible] | Do | Do | Do | Almost complete take. No slough of axillary flap. Discharged with small granulating area. |
| M[illegible] | Do | Do | Do | Take of centre of graft. Serum under remaining part. Slough of tip of axillary flap. Discharged with granulating area. |
| [illegible] | Do | Do | Do | Almost complete take. Slough of tip of axillary flap. Wound infected. Discharged with small granulating area. |
| [illegible] | Do | Do | Do | Almost complete take. Slight slough of skin edges. Pyocyaneus infection. No slough of axillary flaps. No discharge now. |

PARTIAL TAKES—CLEAN CASES—Continued

| SEX AND AGE | [illegible] | [illegible] | [illegible] | REMARKS |
|---|---|---|---|---|
| F. 30 | Ulcer of breast; extensive [illegible] complete [illegible] | Immediate [illegible] Thiersch | Silver foil | More than ⅔ take. No slough of axillary flap. Discharged with small granulating area. |
| F. 37 | Do. | Do. | Do. | Take of 9/10 of graft. Slough of tip of axillary flap. Discharged with small granulating area. |
| F. 38 | Do. | Do. | Do. | Take of small portion of graft. No slough of axillary flap. Discharged with granulating wound. Admitted to hospital. |
| F. 39 | Ulcer of breast; [illegible] complete [illegible] Ulcer [illegible] [illegible] Admitted | Do. | Do. | Take [illegible] seemed boggy and about to slough at first dressing. No slough of axillary flap. Discharged with granulating wound. |
| F. 42 | Ulcer of breast; operation [illegible] | Thiersch and several grafting [illegible] Thiersch | Wet gauze. Soft [illegible] Rubber protective | Thiersch grafting almost complete. Two small grafts [illegible] result |
| F. 48 | Do. | Admitted to Thiersch | Do. | Grafted 3 months after breast operation. Almost complete take. Very little [illegible] sloughed. Nearly healed when discharged |
| F. 48 | Do. | Do. | Rubber protective Dry gauze | Graft [illegible] Almost complete take. Healed when discharged. |
| F. 45 | Do. | Do. | Do. | Almost complete take. Nearly healed when [illegible] operation |
| F. 46 | Do. | Do. | Silver foil | Almost complete take. Nearly healed when discharged. |
| F. 60 | Do. | Do. | Do. | Dressed with [illegible] Healed rapidly when discharged |
| F. 49 | Do. | Do. | Do. | [illegible] Discharged [illegible] granulating [illegible] |
| F. 49 | Do. | Do. | Do. | [illegible] Almost healed when discharged 16 days later. |
| F. 53 | Do. | Do. | Do. | Almost complete take. Healed when discharged. |
| F. 41 | Do. | Do. | Do. | Almost [illegible] Many [illegible] Healed when discharged 10 days later |

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|---|---|---|---|---|---|
| | | | | | ings, isolation whole thickness, sessile flaps. Sixth, eleventh and twelfth grattings. Do. dermis Thiersch. |

PARTIAL TAKES. FLOOR OF LIP.

| | | | | | |
|---|---|---|---|---|---|
| M. 4 | Thiersch. Excepted | Antiseptic. Thiersch. | Wet gauze. Salt solution. Rubber protective. | Thiersch. Grafts. Small nos. | Healed. Well. Discharged weeks later. |
| M. 56. | Do. | Do. | Do. | | Take of two islands. Healed. Well. Discharged 10 weeks later. |
| [illegible] | Thiersch. [illegible] | Do. | Do. | Thiersch. [illegible] | Healed. Well. Discharged [illegible] weeks later. |
| M. [illegible] | Do. | Do. | Salt solution. | | Almost complete take. Nose. Healed. Well. Discharged 17 days after [illegible]. |
| M. [illegible] | Do. | Do. | Do. | | Almost complete take. Nose. Healed. Well. |
| M. [illegible] | Do. | Do. | Do. | | Take of small portion of graft. Healed. Well. Discharged 10 days later. |
| M. [illegible] | Do. | Do. | Do. | | One graft taken. Lip completely epithelized after [illegible]. Healed. Well. Discharged. |
| M. [illegible] | Do. | Do. | Do. | | Young [illegible]. Almost complete take. Healed. Well. Discharged [illegible] days after [illegible]. |
| E. [illegible] | Do. | Do. | Not stated. | | Large excision. [illegible]. Wound, infected. Dressed with [illegible]. Healed. Well. Discharged [illegible] days after [illegible]. Condition improved. |
| M. [illegible] | Do. | Thiersch. [illegible] | Salt solution. | | Take of only a few islands. Discharged with [illegible]. |

PARTIAL TAKES—ULCER OF LEG. Continued.

| SEX AND AGE | FOR RELIEF OF | KIND OF GRAFT. | DRESSING. | REMARKS |
|---|---|---|---|---|
| F. 80 | Ulcer of leg (chronic). | Isodermic Thiersch. | Silver foil. | Take, in places. Patient died 8 days after operation. |
| M. 44 | Ulcer of leg (large gu dle). | First and second grattings . autoderma. Thiersch. | .Do. | First partial grafting almost complete take. Few small granulating areas. Second grafting more than ½ take. Discharged much improved. |
| M. 50 | Ulcer of leg (varicose) | Autodermic Thiersch. | Do | About ½ take. Ligation of veins. Wound sluggish. Discharged with granulating area. |
| M. 25 | Do | Do | Do | One-half take. No discharge note. |
| F. 30 | Do | Do | Do | Almost complete take. Healed when dis charged 1 month after operation. |
| F. 43 | Do | Do | Do | Almost complete take. Discharged with 2 small granulating areas. |
| M. 28 | Do, following typhoid | Do | Do | Almost complete take. Small clot under portion of graft. Healed when discharged 6 weeks later. |
| F. 42 | Do | Do | Do | Center of graft sloughed. Healed when dis charged. |
| F. 33 | Do | Do | Do | Excision of veins. One-half take. Healed when discharged. |
| M. 60 | Do | Do | Do | Excision of veins. Two-thirds take. Healed when discharged. |
| M. 58 | Do | Do | Do | Excision of veins. Wound infected. Healed when discharged. |
| F. 6 | Do | Do | Not stated. | Graft cut by freezing external cutaneous nerve of thigh. Almost complete take. Healed when discharged. |

PARTIAL TAKES—MISCELLANEOUS ULCERS.

| | | | | |
|---|---|---|---|---|
| M. 40 | Ulcer following burn (popliteal space) | Autodermic Thiersch. | Wet gauze. Salt solution. Rubber protective. | Grafts varied in thickness. 8 pieces used. About ½ take. Thin grafts took best. Almost healed when discharged 51 days later. |
| M. 11 | Do (arm, face, hand and | Do | Do | Take of small islands. Almost healed when |

| | | | | | |
|---|---|---|---|---|---|
| M. | Do. (ankle). | ... ...Do..... | ..... | .....Do..... | One-half take. No discharge note. |
| F. 40 | Do. (body and arms). | ... ...Do..... | ..... | ...Do..... | Almost complete take. Almost healed when discharged. |
| F. 32 | Do. (foot). | .....Do..... | ..... | ...Do..... | Almost complete take. Healed when discharged. |
| F. 24 | Do. (thigh). | ... ...Do... | ..... | ...Do..... | Almost complete take of both ulcers at first dressing. Wound infected. ¼ of lower graft sloughed. Healed when discharged. |
| F. 57 | Do. (hip). | ... ...Do..... | ..... | ...Do..... | X-ray burn. About ⅓ take. Healed when discharged 5 weeks later. |
| F. 24 | Do. (hand). | ....Do..... | ..... | ...Do..... | Almost complete take. Nearly healed when discharged. |
| M. 31 | Do. (forearm). | ....Do..... | ..... | ...Do..... | Almost complete take. Several small granulating areas when discharged. |
| F. 5 | Do. (thigh and abdomen). | Isodermic Thiersch | ..... | Do..... | Two-thirds take. Graft from child's father. Discharged with granulating wounds. |
| F. 4 | Do. (neck, face and hand). | First grafting autodermic Thiersch. Second grafting isodermic Thiersch | ..... | ...Do..... | First grafting large area covered. More than ⅓ take. Second grafting take of only small portion. Almost healed when discharged. |
| M. 39 | Do. (legs). | ... ...Do..... | ..... | .....Do..... | Take of only a few islands of each grafting. Wound healing rapidly when discharged. |
| M. 17 | Do. (arm and body). | First and second graftings autodermic Thiersch. | Not stated. | | First grafting almost total failure. Take of few islands. Second grafting almost complete take. Healed when discharged. |
| F. 17 | Do. (arm and axilla). | Do..... | ..... | ...Do..... | First grafting more than ⅓ take. Second grafting cut under ether spray. More than ½ take. Transferred to medical side with typhoid fever. Healed when discharged. |
| F. 44 | Ulcer and contraction following burn. | First grafting isodermic Thiersch. Second and third graftings autodermic Thiersch. | Silver foil. | | First grafting over ulcer and defect following plastic operation. Second grafting ¼ take. Third grafting take of only a few islands. Patient left hospital against advice. |
| M. 45 | Ulcer following excision of carbuncle on neck. | ....Do..... | ..... | ...Do..... | Ulcer 6 x 6 cm. Granulations excised. Nearly complete take. Discharged with small granulating area 16 days later. |
| M. 50 | Do. ..... | ...Do..... | ..... | Do..... | Ten days after excision of carbuncle the granulations were excised, and grafts applied. Take of few islands. Discharged with large granulating wound. |

PARTIAL TAKES—MISCELLANEOUS ULCERS—Continued.

| SEX AND AGE. | SITE AND ETIOLOGY. | GRAFTING. | DRESSING. | REMARKS. |
|---|---|---|---|---|
| M. [illegible] | Ulcer, post traumatic (both legs). | First grafting isodermic Thiersch. Second and third grafting autodermic Thiersch. | Silver foil. | Slight slough of graft on left heel. Patient got out of bed and walked about the day following [illegible]. Healed when discharged. |
| M. 51 | Do. (heel). | Do. | Do. | Two-thirds take. Discharged 6 weeks later with small granulating area [illegible]. |
| M. 29 | Do. (ankle). | Do. | Do. | Two-thirds take. No [illegible]. |
| M. 36 | Do. (ankle). | Do. | Do. | Flap [illegible] Healed when discharged [illegible]. |
| M. 41 | Do. (leg). | Do. | Do. | Almost complete take. Healed when discharged. |
| M. 37 | Do. (leg). | Do. | Do. | Almost complete take. Few small sloughs at edge of wound. Discharged with small granulating area. |
| M. 38 | Do. (leg). | Do. | Do. | Almost complete take. Healed when discharged. |
| [illegible] | Do. (leg). | Do. | Do. | [illegible] Healed when discharged. |
| F. 66 | Do. (leg). | Do. | Wet gauze. Solution. Rubber protective. | Take of few islands. Little benefit from operation. |
| M. 39 | Do. (thigh). | Do. | Do. | Almost complete take. Pulmonary embolus followed operation. Healed when discharged. |
| M. 28 | Ulcer following [illegible] healed tuberculosis. | Do. | Do. | Wound 10 x 10 cm. Almost complete take. Discharged with granulating wound. |
| M. 24 | Ulcer following excision of tarsus. | Do. | Silver foil. | Almost complete take. Graft put immediately on recipe. Advised [illegible] Discharged with granulating area. |
| F. 7. | Ulcer following plastic operation arm and axilla. | First and second grafting autodermic Thiersch. | Do. | First grafting on arm, no note. Second grafting on axilla, no note. Discharged with granulating area. |
| F. 37. | Ulcer (hip). | Autodermic Thiersch. | Do. | Wound [illegible] Fatal [illegible] new clot. Sudden death [illegible] days after [illegible]. |
| M. 39 | Ulcer (thigh). | Do. | Do. | Almost complete take. Discharged with |

| | | | | | |
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| | | operation. | | | take. Plastic flap sloughed. Healed when discharged. |
| M. H. | | Ulcer of leg (tuberculous). | Do. | D. | Plastic. Defect grafted. One-half take. Blood clot under remainder of graft. No discharge note. |
| M. [illegible] | | Ulcer of thigh (epitheliomatous). | Do. | D. | Third admission. Almost complete take. Discharged with small granulating area. |
| M. [illegible] | | Do. | Do. | D. | Almost complete take. Discharged with small granulating area. Fourth admission. Graft of third broke down. |
| L. [illegible] | | Ulcer of back and temple (epitheliomatous). | D. | D. | Looked like total failure at first dressing. Some of graft lived, however. Healed when discharged 3 weeks later. |
| M. [illegible] | | Ulcer (thigh). | D. | D. | Seven-eighths take. Healed when discharged. |
| M. [illegible] | | Ulcer (popliteal space). | D. | Rubber protective. Dry gauze. | D. Most [illegible]. Blood clot under remainder. Discharged with 1 or 2 small granulating areas. |
| M. [illegible] | | Ulcer following infection of foot. | D. | Silver foil. | Wound 7 [illegible]. Almost complete take. Discharged with 1 or 2 small granulating areas. Returned one year later with keloid in edges of grafted area where he had been rubbed. There was also a tendency to keloid formation in the wound from which the grafts were cut. The grafts were movable. |
| M. [illegible] | | Ulcer following wound of leg. | Do. | .....Do..... | Two-thirds take. Healed when discharged. |
| M. [illegible] | | Ulcer following removal of lip. | Do. | Protective. Dry gauze and moss pad. | Almost complete take. The ulcer was excised the day graft cut without any attempt to [illegible]. Tissue was simply sutured on that side following the incision. Healed when discharged. |

PARTIAL TAKES—CONTRACTIONS.

| | | | | | |
|---|---|---|---|---|---|
| F. [illegible] | | Contracting ulcer of leg. Varicose veins. Healed. Last admission, with [illegible] and chronic. | Do. | Not dated. | Last admission, [illegible]. Several admissions, grafts varied in number. Almost complete take. Discharged with small granulating area. Two subsequent admissions, without grafting. |
| M. [illegible] | | Ulcer [illegible]. | Do. | D. | Two-thirds take. Blood clot under remainder. Nearly healed when discharged. |

PARTIAL TAKES. CONTRACTIONS. Continued

| SEX AND AGE. | FOR RELIEF OF. | KIND OF GRAFT. | DRESSING. | REMARKS. |
|---|---|---|---|---|
| F. 4 | Contraction following burn (head and neck). | Autodermic Thiersch. | Silver foil. | Plastic, successful. Defect grafted. Almost complete take. Healed when discharged 2 months later. |
| F. 26 | Do. (neck). | Do. | Do. | Plastic, successful. Defect grafted. Complete take except around edges. Healed when discharged 2 weeks later. |
| M. 25 | Do. (arm and axilla). | Do. | Do. | Plastic, successful. Defect grafted. Almost complete take. Nearly healed when discharged. |
| F. 9 | Do. (hand and elbow). | Do. | Do. | About ½ take, on hand. Almost complete take on elbow. Healed when discharged a month later. |
| F. 6 | Do. (face). | Do. | Do. | Plastic, successful. Defect grafted. About ½ take. Healed when discharged. Later admission for plastic. No grafting. |
| M. 7 | Do. (foot). | Do. | Do. | Almost complete take. Healed when discharged. |
| F. 2 | Do. (hand). | Do. | Do. | Plastic. Defect grafted. No note on result. Transferred to medical side. |
| F. 29 | Do. (neck and breast). | First and second grafts. Autodermic Thiersch. | Do. | Plastic. Defect grafted. Flap and graft both partially sloughed. Second grafting. ¾ take. Discharged with small granulating area. |
| M. 47 | Dupuytren's contraction. | Autodermic Thiersch. | Rubber protective. Dry gauze. | Take of few islands. Clot under graft. Radial nerve cut. Healed when discharged 6 weeks later. |
| M. 33 | Contraction following injury (nose and eyelids). | Autodermic whole thickness. | Silver foil. | Plastic. Whole-thickness graft. Take of small part of graft on nose. Discharged improved. |
| M. 47 | Defect following operation for sarcoma of soft parts (shoulder). | Immediate autodermic Thiersch. | Protective dry gauze. | Almost complete take. Grafts applied directly on the muscles. Healed when discharged. |
| M. 6 | Contraction following burn (axilla). | Do. | Silver foil. | Plastic and defect grafted. Almost complete take. Rise of temperature. Cough. Discharged with small granulating area. |

COMPLETE AND PARTIAL TAKES.

| | | | | |
|---|---|---|---|---|
| F. 60 | Defect following operation for carcinoma of | First grafting immediate autodermic Thiersch. | Silver foil. | Wound 10 x 10 cm. First grafting ⅓ take. Slough of tip of axillary flap. Second |

| | | | | | |
|---|---|---|---|---|---|
| | | | autodermic Thiersch. | tective. | nearly complete take. Second grafting complete take. Healed when discharged. |
| F. 19. | ... | Contracted scar (lip and hand). | Autodermic Thiersch. | Silver foil. | Graft on finger complete take. Graft on lip almost complete take. Discharged with small granulating area. |
| F. 18. | ... | Contraction following burn (hands). | ...Do... | ...Do... | Plastic. Defect grafted. Left hand complete take. Right hand ½ take. Healed when discharged. |
| M. 9. | ... | Do. (chin, face, neck, chest and hands). | First and second graftings autodermic Thiersch. Third grafting autodermic whole-thickness. | ...Do... | Plastic. Defect grafted. First and second graftings partial take. Third grafting complete take. Living flap from arm complete take. Healed when discharged. |
| M. 11. | ... | Ulcer following burn (arms, chin and neck). | Autodermic Thiersch. | ...Do... | Three wounds grafted. Complete take of two. Small slough of third. Healed when discharged. |
| M. 20. | ..... | Do. (arm and back). | Isodermic Thiersch. | ...Do... | One ulcer complete take. Other take of only center. Rapid spread of epithelium. Nearly healed when discharged 17 days later. |
| M. 14. | ... | Do. (arm, legs and trunk). | First grafting autodermic Thiersch. Second, third, fourth, fifth, sixth, seventh and eighth graftings isodermic Thiersch. | .....Do..... | Very large area to cover. 31 pieces of skin used besides numerous small bits obtained by Reverdin's epidermic method. First grafting more than ⅔ take. Second, third, fourth, fifth and sixth graftings complete take. Seventh ½ take. Eighth ¼ take. Discharged with few small granulating areas. |
| M. 28. | ... | Do. (leg). | First, second, third and fourth graftings autodermic Thiersch. | Wet gauze. Rubber protective. | First grafting ½ take. Second and third graftings appeared to be complete takes, but later broke down in places. Fourth grafting complete take. In hospital 6 months. There was an atypical growth of epithelium. Healed when discharged. Returned later for amputation. |
| M. 5. | .... | Ulcer of stump following amputation (leg). | First grafting isodermic Thiersch (brother). Second grafting autodermic Thiersch. | Rubber protective. Dry gauze. | First grafting ⅔ take. Serum under remainder of graft. Pyocyaneus infection. Second grafting complete take. Healed when discharged. |
| F. 68. | ... | Ulcer (leg, varicose). | Isodermic Thiersch. | Silver foil. | Ligation of veins. Graft used was half-hour old and was edematous from soaking in salt solution. Graft on small ulcer complete take. Graft on large ulcer partial take. Discharged improved. |

## COMPLETE AND PARTIAL TAKES—Continued.

| SEX AND AGE. | SORE HEALED. | KIND OF GRAFT. | DRESSING. | REMARKS. |
|---|---|---|---|---|
| F. 50. | Ulcer (leg, varicose). | First grafting isodermo Thiersch (whites). Second grafting autoderm. Reverdin. Third grafting isodermo Thiersch. | Silver foil. | Frankenheim's operation. Two weeks' interval, and later healed over. First grafting almost entirely lost. Complete take. Later grafts partial takes. Second grafting, no pinch graft. Complete take. Third grafting, almost complete take. Healed when measured. |
| M. | Compound comminuted fracture of humerus, with extensive laceration of soft parts. | First grafting autoderm. Thiersch, whole thickness, living flap. Second and third graftings autoderm. Thiersch. | Hot boric solution, compresses. Silver foil. | Complete take of flap from arm, and graft at first redressing. Third grafting, skin left on amputation stump. Loss of flap. Almost complete take. Discharged with small granulating area. |

## PARTIAL TAKES AND FAILURES.

| | | | | |
|---|---|---|---|---|
| F. 40. | Defect following operation for carcinoma of breast. | First and fourth graftings autoderm. Thiersch. Second and third graftings isodermo Thiersch. | Silver foil. | First grafting, 3 days. Slough of flap and yellow flap. Second grafting, 12 days. Third grafting, take a few days. Fourth graft, 3 days. Thrombosis of median basilic vein observed. Pinches of flap at this date. Discharged with small granulating area. |

## COMPLETE AND PARTIAL TAKES AND FAILURES.

| | | | | |
|---|---|---|---|---|
| F. 20. | Defect following operation for carcinoma of breast. | First grafting isomeshes autoderm. Thiersch. Second and third graftings isodermo Thiersch. | Silver foil. | First grafting, 10 days. No graft left but living flap. Second grafting, same. Third grafting, complete take. Healed when measured. |
| F. 49. | Ulcer of both legs (varicose). | First grafting autoderm. Thiersch. Second grafting isodermo Thiersch. | Do. | Veins not excised. Grafted 30 years ago. Ulcer broke down 8 years later. First grafting, no clear takes, other clear takes. Second grafting, complete take. No discharge. |
| F. 55. (Col.). | Ulcer (both legs, varicose). | First grafting autoderm. Thiersch. Second grafting autoderm. Reverdin (blisters from). Third and fourth graftings isodermo Thiersch (from white women). Fifth grafting autoderm. Reverdin. Sixth | Do. | First grafting, 11 days after Trendelenburg's operation, complete take. Second grafting, 15 days. Third grafting, complete take. Fourth grafting, partial take. Fifth grafting, 10 days after. Sixth grafting, 12 days. Discharged with area 1 cm. in diameter not healed. Returned 3 weeks later with recurrence. Re-amputated. |

| | | | | | |
|---|---|---|---|---|---|
| [illegible] | [illegible] | [illegible] | [illegible] | [illegible] | [illegible] |
| [illegible] | Do. | Do. | Do. | [illegible] | [illegible] |
| [illegible] | Do. | Do. | Do. | [illegible] | [illegible] |
| [illegible] | Do. | Do. | Do. | [illegible] | [illegible] |
| [illegible] | [illegible] | Do. | Do. | [illegible] | [illegible] |
| [illegible] | [illegible] | [illegible] | Do. | [illegible] | [illegible] |
| [illegible] | [illegible] | [illegible] | Do. | [illegible] | [illegible] |
| [illegible] | [illegible] | [illegible] | [illegible] | [illegible] | [illegible] |
| [illegible] | [illegible] | [illegible] | [illegible] | [illegible] | [illegible] |
| [illegible] | [illegible] | [illegible] | [illegible] | [illegible] | [illegible] |
| [illegible] | [illegible] | [illegible] | [illegible] | [illegible] | [illegible] |
| [illegible] | [illegible] | [illegible] | [illegible] | [illegible] | [illegible] |
| [illegible] | [illegible] | [illegible] | [illegible] | [illegible] | [illegible] |

### Summary of Complete Takes.

There are 188 complete takes of graftings for *the relief of the defect following the complete operation for carcinoma of the breast. Clean cases:* 176 immediate grafts. *Ulcer following:* 12 secondary grafts. *Variety of grafts:* 187 autodermic Thiersch and 1 isodermic Thiersch. *Dressings:* 179 silver foil, 6 not stated, 2 gauze, wet with normal salt solution and covered by rubber protective; 1 rubber protective and dry gauze. All were healed when discharged. There was slough of the tip of the axillary flap in a considerable number of these, without affecting the grafts, and this with other complications, in many cases, prolonged the stay in the hospital.

*Complications.*—There were several cases of pleurisy and pneumonia following operation. There was a case of pyocyaneus infection with complete take of the grafts, and a streptococcus infection with death on the eighteenth day, although the graft was intact. Phlebitis of the long saphenous vein followed once or twice the cutting of the graft from the left thigh.

*For the Relief of Leg Ulcers.*—62 cases. *Variety of grafts:* 60 autodermic Thiersch; 2 isodermic Thiersch. *Dressings:* 33 silver foil; 5 not stated; 17 gauze, wet with normal salt solution, covered by rubber protective; 7 rubber protective and dry gauze. All were healed when discharged. Plastics were done on some of these cases by sliding flaps from the neighboring skin, and the defect and uncovered portions grafted.

Where there are varicose veins, excision or ligation seems to aid somewhat in the healing. The grafted area over leg ulcers after complete healing of thin grafts often breaks down. Cases are noted in which this has occurred from three weeks to ten years after discharge. Thus it seems best to use thick grafts in this location. Many of the leg ulcer cases were also affected with chronic diseases such as nephritis.

*For the Relief of Other Ulcers.*—30 cases. *Variety of grafts:* 26 autodermic Thiersch; 3 isodermic Thiersch; 1 autodermic Thiersch and living flap. *Dressings:* 20 silver foil; 3 not stated; 4 gauze wet with normal salt solution covered by rubber protective; 2 rubber protective and dry gauze; 1 olive oil and rubber protective.

These ulcers were either tuberculous or they followed burns, injuries, etc. Plastics were done where necessary.

In one case following injury to the lower lip, a flap was turned back from the arm and secured. The raw surface and defect were then grafted with Thiersch grafts, later the living flap was attached at its edges to the lip, and still later the pedicle was separated.

*For the Relief of Contractions.*—57 cases. *Variety of grafts:* 41 autodermic Thiersch; 2 isodermic Thiersch; 8 autodermic whole-thickness sessile flap; 6 autodermic whole-thickness living flap. *Dressings:* 31 silver foil; 5 not stated; 17 gauze wet with normal salt solution with frequent changes, covered by rubber protective; 2 gauze wet with bichloride of mercury, and rubber protective; 2 rubber protective and dry gauze.

These contractions followed burns and injuries, and there were also several Dupuytren's contractions. Plastics were necessary in many of them, and the defect was grafted.

There was a recurrence of contraction in several cases under Thiersch grafts, this being especially noticed in the palm of the hand.

In one case there was a whole-thickness living flap from one side of the abdomen to a part of the hand, and later a second similar flap from the other side of the abdomen.

*For the Relief of Defects Following Excisions of Fibroma of the Scalp, Keloids, Epithelioma of the Eyelid, Carcinoma of the Nose, Lymphangioma of the Thigh.*—8 cases. *Variety of grafts:* 5 autodermic Thiersch; 1 isodermic Thiersch; 1 autodermic whole-thickness sessile flap; 1 autodermic whole-thickness living flap. *Dressings:* 7 silver foil; 1 gauze, wet with normal salt solution, covered by rubber protective.

Several weeks after the amputation of the nose for carcinoma, a whole-thickness living flap was turned back from the forearm, and kept stretched. The defect left by raising the flap was grafted by the Thiersch method, as was also the raw surface of the flap itself. There was complete take of both grafts. Six weeks later the flap was attached to the nasal defect with complete success, and the pedicle was divided two weeks after this.

In one case the Thiersch grafts were placed on muscle and fascia. When seen three years later the grafted area was still closely adherent to the muscle, although the skin was normal in appearance.

*Résumé of Complete Takes.*—345 complete takes, 94 males, 251 females. *Variety of grafts:* 319 autodermic Thiersch; 9 isodermic

Thiersch; 9 autodermic sessile whole-thickness flaps; 7 autodermic whole-thickness living flaps; 1 autodermic Thiersch and living flap. *Dressings:* 270 silver foil; 41 gauze, wet with normal salt solution, covered by rubber protective; 19 not stated; 12 rubber protective and dry gauze; 2 gauze, wet with bichloride and rubber protective; 1 olive oil and rubber protective.

SUMMARY OF PARTIAL TAKES.

*For the Relief of the Defect Following Operation for Carcinoma of the Breast.*—69 clean cases, all females. *Variety of grafts:* 68 immediate autodermic Thiersch; 1 case was regrafted: 1 autodermic and isodermic Thiersch. *Dressings:* 69 silver foil.

*Condition of the Axillary Flap.*—Of the 69 cases there was slough in 20. In these 20 cases there was slough of only the tip of the axillary flap in 13 cases, and more extensive slough in 7 cases.

*Amount of Take.*—46 cases, almost complete take; in 9 of these there was slough of the axillary flap; in 9, $\frac{3}{4}$ take and over; in 4 there was slough of the axillary flap; in 11, $\frac{1}{2}$ take or less; in 6 there was slough of the axillary flap; in 2, take of a few islands; in neither of these last 2 was there slough of the axillary flap. In one case the amount of take was not stated and there was no slough of the axillary flap.

*Condition of Wound when Discharged from Hospital.*—44 cases with granulating wounds, for the most part small; 22 healed; 3 no discharge note.

In one case, where there was take of only a few islands, there was no wound infection nor slough of the axillary flap and nothing to account for such a result except possibly too much pressure by the dressing on the grafted area. On the other hand, there was a $\frac{1}{4}$ and a $\frac{1}{2}$ take with wound infection and slough of the axillary flap.

In some of these cases partial takes can be accounted for by the slipping of portions of the graft with the dressings, or the accumulation of blood and serum under part of the graft, or wound infections, or too much pressure on the newly grafted area by the dressings, and possibly also by the heat of a thick and heavy dressing. It is to be borne in mind that the general condition of a patient has a marked effect on the success of the graft.

The value of grafting in these cases, even with only partial take, is to be emphasized. For example, a wound 10 x 15 cm., with partial take, patient discharged 18 days after operation, with two small granulating areas; wound 15 x 15 cm., healed 26 days after operation; wound 9 x 12 cm., closing rapidly when discharged 15 days after operation.

The notes on the relative size of the grafted area at the time of the operation and later are very few. However, these may be mentioned; at time of operation, 10 x 12 cm., when discharged healed, 7 x 11 cm. At time of operation, 10 x 12½ x 9½ cm. (irregular shape), when discharged healed, 9 x 10¼ x 9 cm. Both of these show considerable shrinkage, even in so short a time.

The notes on the movability of the graft, after some time had elapsed, are also meager, but among these may be mentioned: after one year, adherent to the ribs, except in lower part; in another, after two years, firmly adherent to ribs, except at margins; while in still another, after several years it is slightly movable over ribs.

*For the Relief of the Defect Following Operation for Ulcerated Carcinoma of the Breast.*—9 cases, 1 male, 8 female. *Variety of grafts:* 9 immediate autodermic Thiersch. *Dressings:* 9 silver foil. *Condition of axillary flap:* slough in 4 cases.

*Amount of Take.*—6 cases almost complete; in 3 of these there was slough of the axillary flap; 1, ⅔ take, with no slough of the axillary flap; 1, ½ take, with slough of the axillary flap; 1, small amount of take, with no slough of the axillary flap.

*Condition of Wound when Discharged from the Hospital.*—8 cases with granulating wounds, for the most part small; 1, no discharge note. In one case of almost complete take, there was a pyocyaneus infection, with no slough of the axillary flap. One wound was 20 x 20 cm., with almost complete take. The only male under this heading had tuberculosis of the breast, and a complete operation was performed. The ulcerated condition before the operation may have had some effect on the result of these graftings.

*For the Relief of Ulcers Following Operation for Carcinoma of the Breast.*—12 cases, all females. *Variety of grafts:* 11 autodermic Thiersch; 1 isodermic Thiersch and isodermic whole-thickness sessile flap (in this case there were 12 grafts applied, 9 being isodermic whole-thickness sessile flaps, all of which were successful, and 3 being isodermic Thiersch grafts, which were only partially successful). One case

grafted twice: first grafting almost complete take; no note of second grafting. *Dressings:* 7, silver foil; 2, gauze, wet with normal salt solution, covered by rubber protective; 2, rubber protective and dry gauze. *Amount of take:* 7, almost complete; 1, $\frac{2}{3}$; 3, $\frac{1}{2}$ or less; 1, take of few islands. *Condition when discharged:* 8, with granulating wounds, for the most part small; 3, healed; 1, no discharge note. These ulcers were grafted from 2 to 12 weeks after the original operation.

*For the Relief of Ulcers of the Leg.*—22 cases, 14 males, 8 females. *Variety of grafts:* 20, autodermic Thiersch; 2, isodermic Thiersch. *Dressings:* 17, silver foil; 3, gauze, wet with normal salt solution, covered by rubber protective; 2, not stated. *Amount of take:* 9, almost complete; 1, $\frac{2}{3}$ and over; 7, $\frac{1}{2}$ or less; 3, take of few islands; 2, amount not stated. *Condition when discharged:* 7, with granulating areas for the most part small; 12, healed; 2, no discharge note; 1, died. 20 of these were varicose and 2 specific ulcers. The one death was sudden, in a woman of 80 years.

*For the Relief of Other Ulcers.*—44 cases, 31 males, 13 females. *Variety of grafts:* 40 autodermic Thiersch; 2 were grafted twice; 1 isodermic Thiersch; 3 autodermic and isodermic Thiersch. The 1st grafting in 2 of these was autodermic and the 2d grafting isodermic. In the 3d the 1st grafting was isodermic and the 2d and 3d graftings were autodermic. *Dressings:* 36, silver foil; 4, gauze, wet with normal salt solution, covered by rubber protective; 2, rubber protective and dry gauze; 2, not stated. *Amount of take.* 19, almost complete; 9, $\frac{2}{3}$ and over; 10, $\frac{1}{2}$ and under; 6, take of few islands. *Condition when discharged:* 23, with granulating wounds for the most part small; 17, healed; 3, no discharge note; 1, died. 16 of these ulcers followed burns, 14 were post-traumatic and 14 were miscellaneous.

Among these cases was one sudden death on the eighteenth day. A pulmonary embolus, with recovery, followed the cutting of a graft. The grafts were placed directly on bone or tendon, with fair results. Several plastics were done. Thin grafts of uniform thickness appeared to take better than thicker, unevenly-cut grafts. We note that blood clots were found under a portion of several grafts. Some of the wounds covered were large (7 x 24, 10 x 16 and 18 x 25 cm.).

Advantage was taken in one case of a sensory paralysis of one side, both to excise the ulcer and cut the graft. In one case a keloid formed

under the graft and along its edge, and a tendency to keloid formation was noticed in the scar of the wound from which the graft was cut.

*For the Relief of Contractions.*—14 cases, 7 males, 7 females. *Variety of grafts:* 13 autodermic Thiersch; 2 were grafted twice; 1 autodermic whole-thickness sessile flap. *Dressings:* 10, silver foil; 2, rubber protective and dry gauze; 2, not stated. *Amount of take:* 8, almost complete; 2, $\frac{3}{4}$ and over; 2, $\frac{1}{2}$ take; 1, take of few islands; 1, not stated. *Condition when discharged:* 6, with granulating wounds for the most part small; 7, healed; 1, no discharge note.

Among these there were 9 plastics, and the defects grafted. Most of the plastics were successful, and all the patients were improved. Practically all of these cases were clean. There was a blood clot under a portion of the graft in 2 cases. In the defect left by excision of the sarcoma of the soft parts listed here the grafts were placed immediately on the muscle.

*Résumé of Partial Takes.*—170 cases, 53 males, 117 females; 83 of these were clean and 87 were ulcers. *Variety of grafts:* 161, autodermic Thiersch; 6 were grafted more than once; 3, isodermic Thiersch; 4, autodermic and isodermic Thiersch; 1, autodermic whole-thickness sessile flap; 1, isodermic Thiersch and isodermic whole-thickness sessile flap. *Dressings:* 149, silver foil; 10, gauze, wet with normal salt solution and covered by rubber protective; 7, rubber protective and dry gauze; 4, not stated. *Amount of take:* 95, almost complete; 22, $\frac{3}{4}$ and over; 35, $\frac{1}{2}$ and less; 13, take of few islands; 5, amount not stated. *Condition when discharged:* 96, with granulating wounds for the most part small; 61, healed; 11, no discharge note; 2, died.

*Summary of Complete and Partial Takes.*—14 cases, 7 males, 7 females. *Variety of grafts:* 5, autodermic Thiersch; 2 of these were grafted more than once; 2, isodermic Thiersch.

Two cases: 1st grafting, immediate autodermic Thiersch; 2d grafting, isodermic Thiersch; both isodermic grafts complete take.

One case: 1st and 2d graftings, autodermic Thiersch; 3d grafting, autodermic whole-thickness living flap.

One case: 1st grafting, isodermic (brother) Thiersch, $\frac{3}{4}$ take; 2d grafting, autodermic Thiersch.

One case: 1st grafting, autodermic Thiersch; 2d to 8th graftings, isodermic Thiersch; 2d to 6th, inclusive, complete takes.

One case: 1st and 3d graftings, isodermic Thiersch, almost complete takes; 2d grafting, autodermic Reverdin, complete take.

One case: 1st grafting, autodermic whole-thickness living flap, complete take; 2d and 3d graftings, autodermic Thiersch, one complete, one almost complete take.

*Dressings.*—10, silver foil: 1, silver foil and hot boric solution; 2, gauze, wet with normal salt solution, covered by rubber protective: 1, rubber protective and dry gauze. *Condition when discharged:* 5, with granulating wounds for the most part small; 9, healed.

*For the Relief of Defect Following Operation for Carcinoma of the Breast.*—2 clean cases. There was slough of the axillary flap in both, with $\frac{1}{2}$ and $\frac{2}{3}$ take of the immediate autodermic Thiersch grafts, and complete take of the secondary isodermic Thiersch grafts.

*For the Relief of Contractions.*—5 cases. In 4 of these plastics were done and the defects grafted. In 2 of these there was a living whole-thickness pedunculated flap from a distant part, with complete take. All grafts were autodermic.

*For the Relief of Ulcers.*—7 cases; 4, following burns; 1, following amputation of the leg; 2, varicose leg ulcers. In one case of extensive burn, 31 large pieces of skin were used, besides numerous small bits obtained by Reverdin's and Lusk's methods. In one of the leg ulcer cases there was an atypical growth of epithelium, and the patient returned later for amputation. Serum collected under part of one graft, and there was a pyocyaneus infection of the same wound, but in spite of this, there was $\frac{2}{3}$ take. Two areas were grafted with an isodermic graft, which was œdematous from soaking in salt solution; on one there was complete take, and on the other partial take.

*Partial Take and Failure.*—1 case, female. *Variety of graft:* 1st and 4th graftings, autodermic Thiersch, both $\frac{1}{2}$ take. Second and 3d graftings, isodermic Thiersch, failure and few islands. *Dressings:* silver foil. *Condition when discharged:* granulating area. This case was for the relief of the defect following a breast operation, and there was slough of the axillary flap, also thrombosis of the median basilic vein on the same side, and pleurisy on the opposite side.

*Summary of Complete Take, Partial Take and Failure.*—3 cases, all females. *Variety of grafts:* 1, breast; 1st grafting, immediate autodermic Thiersch, $\frac{2}{3}$ take; 2d and 3d graftings, isodermic Thiersch, 1 failure, 1 complete take. One case leg ulcer; 1st grafting, autodermic

Thiersch, 1 take; 2d grafting, isodermic Thiersch, complete take. One case leg ulcer: 1st grafting, autodermic Thiersch, complete take; 2d grafting, autodermic Lusk, 1 take; 3d, 4th and 6th graftings, isodermic Thiersch (from white women), complete take, partial take and failure; 5th grafting, autodermic Reverdin, partial take. *Dressings:* 3, silver foil. *Condition when discharged:* 1, with granulating wound; 1, healed; 1, no discharge note.

*Summary of Failures.*—17 cases, 11 males, 6 females. *Variety of grafts:* 13 autodermic Thiersch, 2 graftings in 1 case; 1 isodermic Thiersch; 1 autodermic whole-thickness sessile flap. One case: 1st grafting, autodermic whole-thickness sessile flap; 2d grafting, autodermic Thiersch. One case [illegible] mucous membrane (dog). *Dressings:* 12, silver foil; 1, gauze, wet with normal salt solution, covered by rubber protective; 1, rubber protective and dry gauze; 1, collodion and protective; 2, not stated. *Condition when discharged:* 14, with granulating wounds; 2, died; 1, not stated; 5 of these cases were for the relief of the defect following complete breast operation. In 3 there was streptococcus infection, 2 resulting in death on the twelfth and eighteenth days. In the other 2, 1 being an ulcerated carcinoma, there was a wound infection, thus accounting for the failures. Seven were for the relief of miscellaneous ulcers, in at least 5 of which there was wound infection after grafting. Four were for the relief of contractions. Plastics were done on 3 of these cases. Cause of failure was not given in 3 cases. Only 3 of the 17 were discharged improved.

### General Summary.

*Taking a general summary* of the cases [illegible] we find that they were 288 breast, 88 leg ulcer, 87 miscellaneous ulcer, 78 contraction and 9 defects following excision of keloids, etc., making a total of 550 cases, of which 285 were females and 165 males. The average age of the complete takes was 42 years, the youngest being 10 months and the oldest 79 years. *Variety of grafts:* 499, autodermic Thiersch; 15, isodermic Thiersch; 10, autodermic and isodermic Thiersch; 11, autodermic wholethickness sessile flaps; 7, autodermic whole-thickness living flaps from distant parts; 3, autodermic Thiersch and living flaps from distant part; 1, autodermic Thiersch and whole-thickness sessile flap; 1, isodermic Thiersch and isodermic whole-thickness sessile flap; 1, autodermic Reverdin and isodermic Thiersch; 1, autodermic

Thiersch and Reverdin and isodermic Thiersch: 1, zoödermic, from dog. Altogether there were 42 cases in which isodermic Thiersch grafts were applied; 24 were complete takes, 16 partial and 5 were failures, thus showing that isodermic grafts are on the whole well worth trying. Twenty thick grafts from distant parts were used, 10 being whole-thickness sessile flaps, with 9 complete takes and 1 partial; and 10 living flaps, with complete take of all these. *Dressings:* 446, silver foil; 54, gauze, wet with normal salt solution, covered by rubber protective; 21, rubber protective and dry gauze; 2, gauze, wet with bichloride; 1, olive oil and protective; 1, collodion and protective; 25, not stated. *Result of grafting:* 345, complete; 170, partial; 14, complete and partial takes; 1, partial take and failure; 3, complete, partial take and failure; 17, failures. *Condition when discharged:* 416, healed; 117, with granulating wounds for the most part small; 13, no note at discharge; 4, died.

Using the 69 partial take breast cases as the base number, we find that the average length of time in the hospital after operation of breast cases, with complete take of immediate skin graft, is about 20 days; partial take, immediate graft, is about 28 days; and where no graft was used, about 35 days. The 69 complete takes were all discharged healed. The partial takes, 22 cases, were healed; 44 cases had small granulating wounds; in 3 cases the result was not stated. Where there was no graft the great majority were discharged with a fairly large granulating area. These figures show that grafting such cases, even if not completely successful, hastened considerably the healing process.

### Comments.

The use of Reverdin grafts on extensive wounds is not advisable. The application of a large number of these grafts is very tedious and although the healing may be rapid the result is unstable and ulcerations often follow. A single large Thiersch graft, on the other hand, will cover an enormous area in comparison with the above. A greater operative procedure is necessary to secure this type of graft, but it is the one generally chosen and gives a much more stable healing. In exposed positions thin grafts should not be used, as whole-thickness grafts undoubtedly give the most stable healing and promise the most satisfactory results in movability, durability and normal appearance.

The vitality of grafts is much greater than is generally supposed, therefore the immediate transference of the graft is unnecessary. Should it be difficult to check the hemorrhage from the surface to be grafted, the graft can be kept and applied on the following day. Grafts may be preserved for a number of days by simple methods, and then successfully transplanted.

The general health of the patient must be taken into consideration when skin grafting is contemplated, and grafts to be successful must only be transplanted onto healthy wounds. The age of the patient has apparently little effect on the healing of the graft, as many of our complete takes were on cases over 60 years old. As a rule grafts do not take well on luetic individuals. No antiseptics must touch the flaps before or after cutting. A general anesthetic is necessary in the majority of cases where large grafts are removed, although grafts of considerable size can be secured after regional analgesia caused by anesthetizing the trunk of the external cutaneous nerve of the thigh. It is best to cover the defect with a single large graft, if possible, as the healing is just as satisfactory as if several small flaps were used, and the scar is much less. Button-holing all grafts over 3 cm. in diameter, both thin and thick, is an exceedingly important point in the technic of skin grafting, as it allows the free escape of any secretions which may collect beneath the grafts, and does not interfere in any way with the final healing. Silver foil immediately over the graft has proved its worth, but it is best to apply it without the paper and not to use alcohol. Temporary moist salt gauze dressings are also very satisfactory. Too much pressure on the newly-grafted area and too voluminous dressings are to be avoided, and my belief is that neither of these facts have been given their due importance. A moulded cage of wire netting over the grafted wounds will prevent this pressure, and allow free access of air.

Grafting, even if only partially successful, in the majority of cases will shorten the time in the hospital and accelerate final healing. Partial grafting definitely stimulates the epithelial growth from the edges of the wound, even though the graft is placed at a considerable distance from these edges. Splinting the grafts with a wide-meshed rubber impregnated material is of considerable advantage, as it prevents slipping and allows observation of the grafts at any time without fear of displacing them. Grafts take as well on clean, healthy, undisturbed

granulations as on fresh wounds. In fact, in many cases grafts will be successful when placed on a clean granulating surface after failure on the same area as a fresh wound. Zoödermic grafts, especially from young dogs (up to about 5 months old), take better than the literature leads one to believe.

In this series of cases autodermic grafts have taken somewhat better than isodermic, but my own personal experience convinces me that isodermic grafts are quite as successful as those from the same individual, under similar favorable conditions; this applies especially to isodermic whole-thickness grafts, although Thiersch grafts have also healed well. When isodermic grafts are used it is of great importance that the individual from whom the grafts are obtained be healthy, as cases of syphilis, tuberculosis and small-pox have been reported as having been transmitted in this way.

Vascular sprouts have been demonstrated in epidermic grafts on the second day, and in cutis grafts on the third day. Under whole thickness grafts a layer of adipose tissue regenerates within a comparatively short time, and this is most important as it prevents future contraction and insures movability.

Sensation begins to be restored to the transplanted skin within a few weeks. The nerve supply comes in from the periphery and not from the underlying tissues. The sensation of touch appears first, then pain, and lastly temperature sense.

When either a thin or thick black graft is applied to a defect on a white person, the pigment disappears sooner or later, and vice versa. Thiersch grafts adhere to the underlying tissues for a much longer time than whole-thickness grafts. The majority of Thiersch grafts, especially on breast cases that I have examined, were still adherent throughout the greater part of their extent. The shrinkage in the size of a wound after grafting is in some cases quite remarkable, and this is also more pronounced where whole-thickness grafts are used than following the use of Thiersch grafts.

Contraction is prevented to a large extent by grafting. It occurs more often in areas grafted by Reverdin's method, although it sometimes occurs under Thiersch grafts on exposed positions, such as the palm of the hand. In such locations the whole-thickness of the skin should be transplanted, in fact, whole thickness grafts should be employed much more extensively than they are at present, as they offer

many advantages and take as well as thin grafts. Sloughing of the axillary flap in breast cases has little effect on the healing of the grafts, as in many of the complete takes there was slough of the flap, and in many of the partial takes there was no slough. Mild wound infections, such as pyocyaneus, seem to have little effect on the ultimate healing of the graft.

Although skin grafting is being utilized each year more and more, nevertheless its value is not yet fully appreciated, and many cases are dressed week after week and allowed to heal by granulation which could be closed by grafting in a much shorter time and with less chance of future cicatricial contraction.

I wish to thank Mr. H. L. Conner, of the fourth-year class, for his help in the experimental work.

## Bibliography.

Abbe. Medical Record, N. Y., October 12, 1878, p. 313.

Agnew. Principles and Practice of Surgery, 1878, Vol. 1, p. 124.

Ballance. Quoted by Dench. Keen's Surgery, Vol. 4, p. 838.

Baronio. Cited by Pollock, and also by Martin.

Bernhard. Deutsche Ztschr. f. Chir., 1905, Bd. 78, p. 574.

Brewer. Medical Record, May 6, 1882, Vol. 21, p. 483.

Browning. Communicated through Dr. Richard Bell.

Brüning. Centralbl. f. Chir., 1904, Bd. 31, p. 881.

Bryant. Operative Surgery, Vol. 1, p. 575.

Bryant, T. Manual for Practice of Surgery, 4th edition, 1885, p. 166.

Büngер. Jour. d. Graefe et Walther, 1823, IV, p. 569.

Burkhardt. Deutsche Ztschr. f. Chir., 1905, Bd. 79, p. 216.

Cannaday. Journal American Medical Association, June 2, 1906, p. 1682.

Carmalt. Reference Hand Book of Medical Sciences, 1888, Vol. 6, p. 457.

Ceconozzi. La Riforma Med. Napoli, November 1, 1909, p. 1205.

Connell. Col. Med. Jour., January, 1910, p. 21.

DaCosta. Modern Surgery, 1904, p. 923.

Davis, G. W. Lancet, London, September 19, 1903, p. 863.

Davis, J. S. Surgery, Gynecology and Obstetrics, November, 1907, p. 554.

Davis, J. S. Annals of Surgery, March, 1909, p. 356.

Davis, J. S. Johns Hopkins Hospital Bull., June, 1909, p. 176.
Davis, J. S. Annals of Surgery, September, 1909, p. 543.
Doolittle. Journal American Medical Association, March 26, 1898, p. 716.
Dowd. Annals of Surgery, February, 1906, p. 278.
Ehrenfried-Cotton. Boston Med. & Sur. Jour., December 23, 1909, p. 911.
Flegenheimer. Virginia Medical Monthly, June 26, 1903.
Finney. Annals of Surgery, July, 1909, p. 324.
Foote. Medical Record, November 9, 1901, p. 750.
Försterling. Centralbl. f. Chir., 1907, Bd. 34, p. 594.
Fowler. Dennis System of Surgery, Vol. 2, p. 144.
Fowler. Treatise on Surgery, 1906, Vol. 1, p. 327.
Freeman. Sajous' Manual and Analytical Encyclopedia of Practical Medicine, 1901, Vol. 6, p. 142.
Galbraith. Illinois Med. Jour., December, 1909, p. 664.
Gerster. Park's Surgery by American Authors, Vol. 2, p. 687.
Girdner. Medical Record, July 30, 1881, Vol. 20, p. 119.
Goldmann. Centralbl. f. Chir., 1906, Bd. 33, p. 793.
Gross. System of Surgery, 1882, Vol. 1, p. 448.
Habhegger. Annals of Surgery, December, 1908, p. 909.
Hacker. Arch. f. Clin. Chir., 1888, Bd. 37, p. 97.
Hagen. Centralbl. f. Chir., 1905, Bd. 32, p. 882.
Hamilton. New York Journal of Medicine, September, 1854, p. 165.
Hayward. Munch. med. Wochenschr., September 7, 1909, p. 1836.
Heckel. J. A. M. A., November 6, 1909, p. 1591.
Hoffmann. Centralbl. f. Chir., 1907, Bd. 34, p. 318.
Isnardi. Centralbl. f. Chir., 1905, Bd. 32, p. 370.
Ivanova. Wien. med. Bl., August 8, 1888.
Jacobson-Steward. Operations of Surgery, 1902, Vol. 1, p. 188.
Johnston, C. Ashurst's International Encyclopedia of Surgery, Vol. 1, p. 537.
Kaehler. Med. Klin., May 31, 1908, No. 22, p. 836.
Karg. Arch. f. Anatomie und Physiologie, 1888, p. 369.
Keen-White. American Text-Book of Surgery, 4th edition, p. 1199.
Kellock. Lancet, November 25, 1899, p. 1434.
Krajcv. Munch. med. Wochenschr., September 22, 1908, Vol. 55, No. 38, p. 1969.

KRAUSE. Sammlung klin. Vorträge, 1896, No. 143.
KUHN. Centralbl. f. Chir., 1907, Bd. 34, p. 358.
LANGENBECK. Cited by Krause.
LANZ. Centralbl. f. Chir., 1908, Bd. 35, p. 3.
LAPLACE. Medical Bulletin, Philadelphia, March, 1908, p. 83.
LAUENSTEIN. Centralbl. f. Chir., 1904, Bd. 31, No. 35.
LAWSON. Transactions of the Clinical Society of London, 1871, p. 49.
LEFORT. Cited by Martin.
LEGG. System of Operative Surgery, Burghard, Vol. 1, 1909, p. 49.
LEXER-BEVAN. General Surgery, 1908, pp. 47 and 133.
LOEB. Bulletin of the Johns Hopkins Hospital, January, 1898.
LOEB-ADDISON. Journal American Medical Association, July 11, 1908, p. 158.
LUSK. Medical Record, December 7, 1895, p. 800.
MACOMBER. Therapeutic Gazette, November 15, 1909, p. 769.
MARCHAND. Deutsche Chirurgie, 1901, pp. 411 and 431.
MARTIN. Thèse de Paris, 1873.
MATAS. International Text-Book of Surgery, Vol. 2, p. 910.
MATHEWSON-PILCHER. Annals of Anatomy and Surgery, 1881, Vol. 3, p. 21.
MAXWELL. Philadelphia Medical Times, October 18, 1873, p. 37.
MEYER. Chicago Medical Journal and Examiner, April, 1877, p. 320.
MILES. Edinburgh Hospital Reports, 1895, p. 647.
MILES. Green's Encyclopedia of Medicine and Surgery, 1908, p. 204.
MIXTER. Boston Medical and Surgical Journal, December 31, 1891, p. 700.
NOESSKE. Deutsche Ztschr. f. Chir., Leipsic, Bd. 83, p. 213.
NYSTROM. Centralbl. f. Chir., 1909, Bd. 36, p. 137.
OLLIER. Bull. de l'Acad. de Méd., Paris, 1872, 2 série, p. 244.
PARK. Modern Surgery, 1907, p. 187.
PARMENTER. Park's Surgery, Vol. 1, p. 277.
PELS-LEUSDEN. Centralbl. f. Chir., 1905, Bd. 32, p. 801.
PERRY. Amer. Jour. of Surg., July, 1909, p. 243.
PILCHER. Annals of Anatomy and Surgery, 1881, Vol. 3, p. 27.
POLLOCK. Transactions of the Clinical Society of London, 1871, p. 37.
PORTER. Journal American Medical Association, January 23, 1909, p. 323.
RENTON. British Medical Journal, June 14, 1890, p. 1367.

Reverdin. Bull. de la Société de Chir., Paris, December 8, 1869.
Reverdin. Archives générales de Méd., 1872, pp. 276, 555 and 703.
Riven. British Medical Journal, November 3, 1877, p. 623.
Robinson. Surgery, Gynecology and Obstetrics, December, 1908, p. 663.
Rosl. Medical Record, November 16, 1907, p. 809.
Schmieden. Centralbl. f. Chir., 1908, Bd. 35, p. 153.
Scott. Southern Med. Jour., January, 1910, p. 46.
Sisk. Kentucky Medical Journal, August, 1908, p. 349.
Socin. Gesellsch. f. Chir., 1888, p. 67.
Stanton. New York State Journal of Medicine, January, 1909, p. 11.
Steinthal. Beiträge z. klin. Chir., 1901, Bd. 29, p. 485.
Stone. Operative Surgery, Bryant & Buck, Vol. 2, p. 910.
Stransky. Cited by Gould in Year Book of Medicine and Surgery, 1901.
Thiersch. Verhandl. der deutsch. Gesellsch. f. Chir., Berlin, 1874, p. 69.
Thiersch. Verhandl. der deutsch. Gesellsch. f. Chir., Berlin, 1886, p. 17.
Thiersch. Verhandl. der deutsch. Gesellsch. f. Chir., Berlin, 1888, p. 66.
Thompson-Miles. Manual of Surgery, 1906, Vol. 1, p. 88.
Tillmans. Text-Book of Surgery, Tilton, 1901, Vol. 1, p. 146.
Torrance. Philadelphia Medical Journal, July 13, 1901, p. 75.
VanMeter. Annals of Surgery, 1890, Vol. 12, p. 193.
Vogel. Centralbl. f. Chir., 1907, Bd. 34, p. 355.
Wagner. Cited by Gould in Year Book of Medicine and Surgery, 1901.
Walsham. Surgery, Its Theory and Practice, 8th edition, p. 39.
Weischer. Centralbl. f. Chir., 1906, Bd. 33, p. 689.
Wentscher. Deutsche Ztschr. f. Chir., 1903, Bd. 70, p. 21.
Wight. Brooklyn Medical Journal, May, 1905, p. 211.
Wise. Hindu System of Medicine, 1860, p. 189.
Wolfe. British Medical Journal, September 18, 1875.
Wolfe. Glasgow Medical Journal, April, 1876.
Wood. Keen's Surgery, 1906, Vol. 1, p. 377.
Young. International Clinics, 1905, Vol. 1, 15th Series, p. 81.

# EPIDEMIC CEREBROSPINAL MENINGITIS AND SERUM THERAPY AT THE JOHNS HOPKINS HOSPITAL.*

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## Introduction.

The detailed report of the results of the application of such a therapeutic measure as the antimeningitis serum (Flexner) is justified by its novelty and importance. Generalized statements and statistical analyses are abundant even at this early date. Indeed, the results[1] in this clinic have already been several times exposed. Flexner's[2] publications upon the subject do themselves seem sufficient. But the story at length of the steps of each individual case in a series is helpful in guiding other clinicians who may perchance have a case to deal with, out of the general run, and may find in this report instances where the treatment, favorable or not, is laid bare for their consideration. The purpose of this paper is to place on record a series of cases of acute epidemic cerebrospinal fever treated by the antimeningitis serum, and the impressions and deductions of those in attendance upon them.

The following index will serve as a guide to the reader and so atone for the length of the paper:

INDEX.

| | | Page |
|---|---|---|
| I. | Results: | |
| | 1. Recovery and Mortality | 398 |
| | 2. Complications | 402 |
| | 3. Sequelæ | 404 |
| II. | The Serum: | |
| | Historical Introduction | 405 |
| | 1. Instruments | 406 |
| | 2. Preparation of Patient | 408 |
| | 3. Pressure in Subarachnoid Space | 408 |

* For permission to present this work I desire to thank Prof. L. F. Barker, in whose service the cases were studied.

II. The Serum—Continued. PAGE
4. Removal of Spinal Fluid . . . . . 408
5. Injection . . . . . 410
6. Amount Injected . . . . . 411
7. Other Applications of the Serum . . . . . 413
8. Anæsthesia . . . . . 414
9. Indications for Serum . . . . . 415
10. Serum Disease and Anaphylaxis . . . . . 415
III. Accessory Treatment:
1. Isolation . . . . . 418
2. Nourishment . . . . . 418
3. Hydrotherapy . . . . . 418
4. Medicines . . . . . 418
IV. The Cases before Treatment with Serum:
1. The Character of the Cases . . . . . 419
2. The Day of the Disease . . . . . 420
3. Age, Color, and Sex . . . . . 421
4. Symptoms . . . . . 422
5. Signs . . . . . 427
6. The Blood . . . . . 429
7. Temperature, Pulse, and Respirations . . . . . 432
8. Confirmation of Clinical Diagnosis . . . . . 434
V. The Effect of the Serum:
1. Temperature Chart . . . . . 437
(a) Temperature . . . . . 437
(b) Pulse . . . . . 447
(c) Respirations . . . . . 447
2. Symptoms . . . . . 448
3. Signs . . . . . 451
4. Spinal Fluid . . . . . 457
(a) Cytologically . . . . . 458
(b) Bacteriologically . . . . . 470
VI. Protocols and Temperature Charts:
Cases I-XXIII, Inclusive . . . . . 478
Bibliography . . . . . 509

## I. Results.

1. Recovery and Mortality.—In the previous history of the Johns Hopkins Hospital, the indexed cases of meningitis in which the *Diplococcus intracellularis meningitidis* was demonstrated number 73. The mortality is 66.6 per cent, figured for 24 deaths. This covers a period of 19 years, during which the cases were treated by repeated lumbar punctures, elimination, and support. The small number of cases

in each individual year render the percentages useless for comparison, as the following table makes evident:

TABLE No. I.—MORTALITY OF CASES IN PREVIOUS NINETEEN YEARS.

| Year. | Cases. | Mortality. | Recovery. |
|---|---|---|---|
| 1893 | 2 | 100.0% (2) | 0 % |
| 1898 | 5 | 80.0% (4) | 20.0% (1) |
| 1899 | 7 | 43.0% (3) | 57.0% (4) |
| 1900 | 4 | 50.0% (2) | 50.0% (2) |
| 1901 | 1 | 0 % | 100.0% (1) |
| 1904 | 1 | 0 % | 100.0% (1) |
| 1905 | 4 | 50.0% (2) | 50.0% (2) |
| 1906 | 3 | 100.0% (3) | 0 % |
| 1907 | 6 | 83.0% (5) | 17.0% (1) |
| Total | 33 | 63.6% (21) | 36.4% (12) |

In no one of these years was there a real, outspoken epidemic. This is fortunate, inasmuch as we consider the cases in this report sporadic, and we wish to compare the results with the above figures. Koplik[7] has only recently emphasized that in considering any mode of therapy for this disease it must be borne in mind that the violence of the infection is much greater in the epidemic than the sporadic type. So the fact that both series in this paper are of sporadic cases renders the results more worthy of comparison.

In the first 6 months of 1908, 23 cases were admitted to the medical clinic, all of which were diagnosed positively by the bacteriological findings. The increased number of admissions is due to the attitude of local physicians, who cannot be given too much credit for enabling a trial of this new therapy. The previous helplessness and hopelessness in the minds of physicians and laymen have made them hasten to take advantage of this new possible chance. This change in attitude has fortunately led them to hurry their cases to the hospital, and has thus given this greater opportunity for trial of the serum. The newspaper advertisement, fruitlessly guarded against, has had this one redeeming feature. The absence of registration of meningitis in Baltimore has made the health board statistics of no value in regard to the apparent increase in the number of cases. But from the character of the cases, and from the fact that but 2 of the 23 had anything in common, locality, occupation, time of outbreak, or other such factors, we feel that the cases in 1908 were truly sporadic and not epidemic.

Of these 23 cases, 19 recovered and 4 died, 82.6 per cent recovery and 17.4 per cent mortality. Such a reversal of statistics is sufficient evidence for the value of the serum. There is no wish to improve these figures by eliminating any of the fatal cases for one reason or another, but a consideration of the 4 is interesting.

The first fatal case, No. IV, was a baby of 29 months, who had been seriously ill for 13 days before admission. He was not sent to the hospital until the onset of a series of convulsions. He did not receive any serum until the fourteenth day of the attack, when he was already unconscious and breathing irregularly. In fact he ceased breathing during the first 24 hours, but was revived by artificial respiration. He died from respiratory paralysis, 48 hours after the first injection of serum, and even in this time the spinal fluid had been rendered sterile.

The second case, No. VII, was of the more fulminant type. He was a man, 26 years old, who was seized with a convulsion while on a spree and never regained consciousness. A right-sided hemiplegia was present on admission. He received serum at the end of the first day, and every 12 hours thereafter until he died on the fourth day. He suffered a series of convulsions and died during the eleventh. The spinal fluid gave abundant growth of diplococci on the first 4 punctures, but the fifth specimen yielded only "five colonies per tube." The serum did not affect his temperature, signs, or symptoms in any apparent way.

The third fatality, No. XIII, was of a colored woman, 25 years old, who received serum first upon the fourth day of the attack. At this time she was also suffering from acute bronchopneumonia of both lungs, and acute myocarditis. She received serum every 12 hours, but died on the sixth day after 3 injections. As in the second case, the temperature, signs, and symptoms were not affected by the serum, but the number of colonies of diplococci recovered from the spinal fluid were reduced from "200 per tube" at the first puncture to "1 per tube" at the third.

The fourth fatal case, No. XXI, developed internal hydrocephalus as a sequela, and died of a respiratory paralysis due to this 52 days after the onset of the meningitis. The spinal fluid had been rendered sterile by three injections of serum. A reappearance of organisms in the spinal fluid on the fortieth day points to the ventricles as their possible habitat in this case, out of reach of intraspinal serum.

On analysis, four noteworthy facts are emphasized:

(1) Case No. IV should have received serum earlier.

(2) The fulminant case, No. VII, was uninfluenced in signs or symptoms by the serum; the reduction in number of diplococci and loss of viability was encouraging.

(3) Complicating infections, as bronchopneumonia in Case No. XIII, hazard the prognosis.

(4) The intraventricular administration of serum must be employed in cases developing internal hydrocephalus, as Case No. XXI.

Flexner and Jobling's * last analysis of 393 cases excluded 43 which were eliminated from the percentages as being one of the following three types:

(1) Cases surviving the dose of serum less than 24 hours;

(2) Rapidly fatal, fulminant cases, as determined by the history and clinical appearance;

(3) Cases of secondary and mixed infections of the meninges, of intercurrent infections, and hopelessly chronic cases moribund after 2 or 3 months' illness.

Of the 393 cases, 295, or 75 per cent, recovered, and 98, or 25 per cent, died. These include cases reported from both the United States and Great Britain. The statistics from the individual clinics show very little variation in results. The larger of those already published are:

TABLE No. II.—RESULTS AT THE DIFFERENT CLINICS.

| Clinic. | Reported by | Cases. | Deaths. | Mortality. | Recovery. |
|---|---|---|---|---|---|
| Children's Hospital, Boston, *et al.* | Dunn [4] | 40 | 9 | 22.5% | 77.5% |
| Belfast Fever Hospitals Purdysburn; Union | Robb [5] | 55 | 16 | 29.0% | 71.0% |
| Edinburgh City Hospital | Ker [6] | 27 | 12 | 44.4% | 55.6% |
| Lakeside Hospital, Cleveland | Ladd [7] | 31 | 11 | 35.5% | 64.5% |
| R. I. Hospital, Providence | Fulton [8] | 22 | 7 | 31.8% | 68.2% |
| Municipal Hospital, Philadelphia | Flexner * | 21 | 9 | 42.9% | 57.1% |
| Mt. Sinai Hospital, New York | Koplik * | 15 | 2 | 13.3% | 86.6% |
| Akron City Hospital, Akron, O. | Chase and Hunt [9] | 12 | 3 | 25.0% | 75.0% |
| City Hospital, Cincinnati | Flexner * (Cole) | 45 | 14 | 31.0% | 69.0% |
| Garfield Hospital, Washington | Morgan and Wilkinson [10] | 10 | 3 | 30.0% | 70.0% |
| Chicago | Churchill [11] | 29 | 13 | 44.0% | 56.0% |
| Portersville, California | Miller and Barber [12] | 4 | 1 | 25.0% | 75.0% |

* Loc. cit.

2. Complications.—The complications of this disease fall into 3 groups:

(1) Those present before the onset, infectious or otherwise, perhaps intensified by the attack:

(2) Those occurring during the disease, but not due to the meningococcus;

(3) Those occurring during the attack, infections by the diplococcus, apparently metastatic from the cerebrospinal fluid, or part of a general infection.

In the *first* group belongs Case No. XII, in which paracentesis tympani was necessary to relieve a double otitis media suppurativa. Inasmuch as there was a history of similar trouble 3 months previous, it was considered a chronic infection intensified, rather than a metastatic infection. The arthritis in Case No. XVI was diagnosed by the orthopedists as "toxic" dependent upon the meningitis, but it was present before the onset of the meningeal symptoms and there was a history of previous attacks. Case No. XXIII had a chronic nephritis which suggested uræmia as a probable diagnosis before lumbar puncture was made. These 3 complications then were present before the attacks of meningitis and should not be counted as complications of the disease itself.

In the *second* group is pneumonia, 2 cases of the lobular type (No. XIII and No. XIV) and 1 of the lobar (No. XVII). The latter was followed by empyema, which was drained by the surgeons. Case No. IX developed an acute fibrinous pleurisy which cleared up rapidly. Acute myocarditis complicated Cases No. VIII and No. XIII, the latter succumbing. In no one of these cases could the diplococcus be demonstrated as directly causing the complication. If the arthritis in Case No. XVI was properly diagnosed as dependent upon the meningitis, it would fall in this group. Central blindness in Case No. V and the right-sided hemiplegia of Case VII belong here.

The common constituent of the metastatic (*third*) group is otitis media, which occurs in all grades, from slight reddening of the drum and deafness to suppuration and rupture. It may be a direct extension from the meningeal infection or a metastasis, but either way it is due to the meningococcus. And the diplococcus can be isolated if paracentesis is done at the proper time, before secondary infection occurs. It is interesting to note that *B. Influenzæ* and *Streptococcus pyogenes* were the invaders isolated in Case No. V, and

may be a sequel of a preceding attack of influenza. Otitis media complicated 4 of the cases, Nos. II, III, V and XVII. In two others, not included, temporary deafness was noted. In Case No. XIV there was a metastatic infection of the right eye, which rapidly developed into a panophthalmitis, resulting in complete loss of sight in that eye. There was no metastatic infection of the joints, though it must be admitted the meningococcus may have localized in the joints of Case No. XVI. There was no purulent arthritis, such as Ladd * reports, and no other local infection where local application of the serum might have been serviceable.

In summary:

TABLE No. III.—COMPLICATIONS IN CASES TREATED WITH SERUM.

| Group I. | | Group II. | | Group III. | |
|---|---|---|---|---|---|
| Complication. | Cases. | Complication. | Cases. | Complication. | Cases. |
| Chronic suppurative otitis media | XII | Broncho-pneumonia | XIII | Otitis media | II |
| Acute arthritis | XVI | | XIV | | III |
| Chronic nephritis. | XXIII | Acute lobar pneumonia | XVII | | V |
| | | Empyema | XVII | | XVII |
| | | Acute fibrinous pleurisy | IX | Panophthalmitis | XIV |
| | | Acute myocarditis. | VIII | | |
| | | | XIII | | |
| | | Central blindness | V | | |
| | | Hemiplegia | VII | | |
| Total cases | 3 | | 9 | | 5 |

In a word, complications attributable to the disease occurred in 10 cases, 43.5 per cent.

With this may be compared the records in the 33 cases of similar type, treated previously to 1908, without serum:

TABLE No. IV.—COMPLICATIONS IN CASES WITHOUT SERUM.

| Group I. | | Group II. | | Group III. | |
|---|---|---|---|---|---|
| Complications. | Cases. | Complications. | Cases. | Complications. | Cases. |
| | | Acute bronchitis | 2 | Otitis media | 5 |
| | | Broncho-pneumonia | 10 | Arthritis | 3 |
| | | Pulmonary œdema | 1 | | |
| | | Acute gastro-enteritis | 1 | | ? |
| | | Acute enteritis | 1 | | ? |
| | | Parotitis | 1 | | ? |
| | | Acute inflammation submaxillary gland. | 1 | | ? |
| | | Hæmorrhagic retinitis. | 1 | | |
| | | Furunculosis | 1 | | |
| | | Paralyses | 2 | | |
| | | Nerve deafness | 2 | | |

* Loc. cit.

Twenty-one of the 33 cases, 63.6 per cent, suffered complications of about the same character as the serum cases. But 18 of these 21 cases died, 85.7 per cent; whereas only 2 of the 10 serum cases with complications (20 per cent) were fatal. Without serum only 2 of the 12 cases to recover had complications; in the serum series, 10 of the 19 surviving cases were complicated.

So we feel justified in saying that not only is the frequency of complications reduced, but also that those which do occur are milder, and do not seriously affect the outcome. In a word, we are more successful now in saving the cases which do suffer complications.

3. Sequelæ.—It is the natural hope that the frequency of sequelæ will keep pace in reduction with the diminished mortality. More terrible than death have been many of the so-called recoveries from the acute attack! We have reference to the type of cases which, dull and apathetic, slowly waste away, or are bedridden with paralysis; imbeciles, deaf, or blind. Undoubtedly internal hydrocephalus is a big factor in most of these cases, and intraventricular puncture and injection of serum early, at the time of the first signs of the trouble, as recently suggested,[13] will help prevent this terrible sequel. Although intraspinal serum probably does not reach in its influence to the lateral ventricles, the rapid subsidence of the spinal infection may prevent spread to those cavities:

Table No. V.—Sequelæ in Cases with and without Serum.

| With Serum. | Case No. | Without Serum. | No. of Cases. |
|---|---|---|---|
| Internal hydrocephalus | XXI | Hydrocephalus | 4 |
| Deafness one ear | III | Deafness | 2 |
| complete | XII | Hemiplegia | 1 |
| Blindness | V | Facial palsy | 1 |
| one eye | XIV | Paralytic squint | 1 |
| Persistent internal strabismus | XI | | |
| Acrocyanosis | XX | | |

The internal hydrocephalus in Case No. XXI at the present time would receive different and, we trust, more hopeful treatment. We have great faith in the prevention of these cases by intraventricular injection of serum early in the severe cases. Case No. III was an obstinate infection and the deafness in one ear must remain as its scar. Case No. XII, however, had a chronic suppurative otitis media.

The complication was present before this attack. Yet it was intensified by the meningitis and complete deafness resulted. The blindness in Case No. V was present on admission to this clinic. Serum earlier might have prevented this terrible sequel. The blindness in one eye (No. XIV) was the result of destruction of the eye by an infection, probably metastatic, of all its structures, directly attributable to the disease, in spite of the serum. The internal strabismus of Case No. XI gives hopes of clearing. It may be far-fetched to hold the meningitis responsible for the acrocyanosis in Case No. XX. It is a tempting possibility, however, and very interesting in that the condition seems to be progressing to an erythromelalgia.[14]

## II. The Serum.

Introduction.—The serum is now well known. It is a specific antiserum produced by immunization of the horse against the diplococcus. It is not standardized as yet, although Jobling[15] believes the opsonic power can be made use of. Similar sera have been prepared elsewhere, but not so successfully employed as yet.

Flexner's first work upon the epidemic type of meningitis was in 1894, when he and Barker,[16] published an extended report of their clinical and pathological study of an epidemic at Lonaconing, Md.

During the New York epidemic of 1904-1905, as a member of the commission appointed by the City Health Department, Flexner undertook the investigation of the pathogenic properties of the meningococcus and the immunization of animals with a view to obtaining immune sera which might be used for the differentiation of the diplococcus by agglutination.

In 1907 three reports appeared detailing the development of his investigations. After a study of the biology[17] of the organisms and of the pathogenesis[18] in the intraperitoneal injection of guinea pigs, he reproduced the lesions and symptoms of cerebrospinal meningitis in man by the introduction of meningococci into the subarachnoid space of monkeys.

The next step was the attempt to prepare an antiserum which would protect these monkeys. He immunized rabbits, goats, and monkeys by successive injections of meningococci and the peritoneal exudate of infected guinea pigs.

The results, he states, were more satisfactory than he expected they would be. With the serum of these immunized animals, first of all.

he protected guinea pigs which had been infected intraperitoneally.[19] Then he protected monkeys by injecting the serum intraspinally at the same time with the living bacteria, and in other cases, several hours later. He saved 4 out of 5 monkeys, whereas all the controls, without serum, died. His conservatism merits the greatest admiration, and his remarks at this stage should be quoted:

"I am far from having any conviction that cerebrospinal meningitis in man can be influenced favorably by injections of immune sera into the spinal canal, or elsewhere in the body. The experiments to be described merely show that guinea pigs and monkeys, in which the conditions of infection can be controlled, can be saved from the otherwise fatal effects of the diplococcus by the use of antisera, and to a less extent by the use of normal sera and other fluids."

While he was doing this work, two papers appeared from German clinics. Kolle and Wassermann,[20] in Berlin, immunized the horse and produced a serum which proved quite effectual in vitro and in animals. A year later Wassermann [21] reported a mortality of 17.3 per cent for 57 cases treated by the subcutaneous injection. He had employed the serum intradurally, and advised this method, but did not pursue it with conviction, it seems to the reader.

Jochmann,[22] in Breslau, prepared a similar serum about the same time (1906), using it intradurally. Schöne [23] reported the apparently good results of the application in a small number of cases.

It was after this, about April, 1907, that Flexner advised the intraspinal injection, in human beings, of the antiserum which he had prepared. To quote his own report, this plan was based upon his observations of its curative action when so applied in monkeys experimentally infected with the meningococcus. The secret of success seems to be in the mode of application, in which the serum reaches the organisms in sufficient concentration to destroy them—a thing not accomplished by the subcutaneous route.

1. Instruments.—The instruments used in making the lumbar punctures and injecting the serum are simple, as shown in the picture (Fig. 1).

(1) *Needles.*—10.5 cm. in length with a bore of 1.5 mm. diameter; a short point, and a butt in which a push connection fits. At first nickel-plated steel needles were used, but after the accident in Case No. XXII the flexible irido-platinum needles were employed exclusively. Three centimeters of rubber tubing serve to connect the needle with the pressure tubes by means of the push connection.

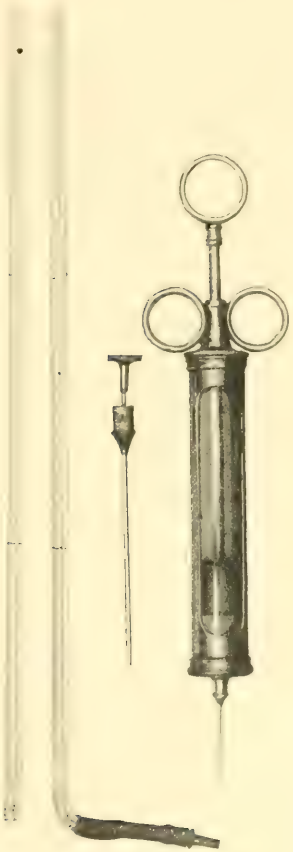


FIG. 1.

(2) *Pressure Tubes.*—They are made in 2 lengths of 400 mm. each, from glass tubing of 6 mm. diameter with a 1 mm. bore. The graduation is marked by rings, every 100 mm.

(3) *The syringe* used for injecting the serum is an ordinary 15 cc. blood-culture syringe. The base of a blood-culture needle serves to connect the syringe with the lumbar puncture needle by the same push connection and rubber tubing which is attached to the pressure tube during removal of fluid.

2. Preparation of Patient.—The patient was always placed upon the left side of the bed, lying upon his own right side. This enabled a right-handed person to work freely. Surgical technique was employed in preparing the site of puncture. The midline is preferred by the author for the introduction of the needle, in adults as well as in children. It is true that the ligamentum supraspinale is tough and difficult to penetrate in adults, and that the subarachnoid space is at a much greater depth, but if care is taken beforehand to pull the knees up and the head down, so that the back is convex and the spines spread apart the subarachnoid space is tapped with ease. This is also easy if the spinal column is straight—seldom the case in a sagging bed without a fracture board or some such support—and if the needle is directed through the fibrous ligament exactly in the midline and introduced carefully in a perpendicular direction.

The interspace chosen is that on the level with the crest of the ileum or the one above it (fourth or third lumbar interspace). The direction is usually a trifle upwards, but one can be guided by the feeling and can avoid sticking the spine above or below, and so not prick the sensitive periosteum.

3. Pressure in the Subarachnoid Space.—The moment fluid appears through the needle, the push connection holding the pressure tube is jointed. The fluid rises to a certain height in this millimeter tube, measured from the level of the spine, and this height is read as the pressure of the fluid in the subarachnoid space. Normally this is from 80 to 130 mm. The second tube can be jointed to the first if it is found the pressure will rise above 400 mm. The pressure, then, is the height to which the fluid will rise in a tube of 1 mm. bore.

4. Removal of Spinal Fluid.—The tube is not disconnected, but the spinal fluid is removed by lowering the end of the pressure tube and allowing the fluid to drop into a sterile, graduated cylinder or test tube or centrifugalizing tube. By this method, at any moment,

the tube can be raised and the pressure in the subarachnoid space read immediately. Here is always a guide to the amount to remove. Inasmuch as serum is to be injected, enough fluid is withdrawn to reduce the pressure well below normal. The amount to accomplish this varies within the widest limits. The following table shows the number of cubic centimeters removed in order to reduce to subnormal the recorded, increased pressures:

TABLE NO. VI.—AMOUNT OF SPINAL FLUID REMOVED TO REDUCE THE PRESSURE TO SUBNORMAL (0-50 MM.).

| Case No. | Fluid removed, in cc. | Pressure before removal. | Case No. | Fluid removed, in cc. | Pressure before removal. | Case No. | Fluid removed, in cc. | Pressure before removal. |
|---|---|---|---|---|---|---|---|---|
| II. | 25 | 400+ | IX. | 31 | 410 | XVIII. | 24 | 330 |
| | 35 | 520 | | 24 | 380 | | 65 | 500 |
| | 20 | 160 | | 28 | 380 | XIX. | 6 | 180 |
| | 20 | 260 | | 15 | 200 | | 18 | 110 |
| III. | 20 | 400 | | 41 | 300 | | 14 | 110 |
| | 40 | 520 | | 45 | 450 | XX. | 30 | 260 |
| | 20 | 375 | X. | 26 | 200 | | 5 | 75 |
| | 46 | 480 | XI. | 30 | 210 | XXI. | 35 | 160 |
| | 50 | 490 | | 16 | 180 | | 65 | 400+ |
| | 60 | 440 | XII. | 34 | 380 | | 50 | 420 |
| IV. | 12 | 180 | | 46 | 200 | | 35 | 250 |
| | 25 | 450 | XIII. | 31 | 600+ | | 50 | 320 |
| V. | 40 | 400 | | 30 | 395 | | 50 | 410 |
| | 20 | 480 | | 19 | 210 | | 50 | 450 |
| | 62 | 300 | XIV. | 23 | 550 | | 45 | 360 |
| | 60 | 250 | | 30 | 400 | | 40 | 650+ |
| VI. | 17 | 170 | | 33 | 500 | | 20 | 200 |
| | 16 | 180 | | 21 | 250 | | 35 | 400 |
| VII. | 30 | 210 | XV. | 30 | 500 | | 40 | 600+ |
| | 35 | 395 | | 45 | 600+ | | 6 | 200 |
| | 49 | 160 | XVI. | 18 | 200 | | 25 | 250 |
| | 35 | 160 | | 20 | 200 | XXII. | 2 | 380 |
| | 30 | 150 | | 12 | 150 | XXIII. | 11 | 400 |
| VIII. | 25 | 400 | | 30 | 510 | | 20 | 250 |
| | 15 | 150 | XVII. | 24 | 300 | | | |
| | 30 | 210 | | 28 | 160 | | | |

These are the records of 75 lumbar punctures. The highest pressure recorded is 650+ mm.—a case (No. XXI) where the fluid rose over the top of a tube 650 mm. in length. The average is 327 mm. It would mean nothing to pick out the lowest pressures, as these figures represent all stages of the disease. The lowest at first puncture is 160 mm., in Case No. XXI, which also was the case to show the highest at any stage. The average at first tap is 330 mm. The average amount of fluid removed in the 75 instances is 30 cc. This was removed to reduce an average pressure of 327 mm. to between 0 and 50 mm.—say to 25 mm. In other words, on the average, 30 cc. of spinal fluid removed succeeded in reducing the intraspinal pressure 300 mm., that is, in general, 1 cc. of spinal fluid is the equivalent of 10 mm. pressure.

An additional advantage in removing the fluid through the pressure tubing is that the rate of flow can be controlled at will by raising or lowering the end of the tube, by making it flow uphill or downhill, until the fluid drops at the proper speed. We differ emphatically with Sachs[24] who, in discussing the measurement of the tension of the spinal fluid, states, "even if such methods be accurate, they are of no more value than observation of the stream by an experienced eye."

It was observed repeatedly that as zero was approached the pulse increased and the respirations became more labored and rapid. This was interpreted as a danger signal and carefully avoided.

5. INJECTION.—After sufficient fluid is allowed to run off, the tubing is disjointed from the rubber connection and the latter clamped with hemostatic forceps. Both hands are free then to fill the syringe with serum. The serum, in its unopened 15 cc. bottles, has been placed previously in a bowl of water at 98-100° F. in order to warm it to body temperature. It is then injected warm by means of the syringe joined to the needle through the rubber connection, as described above. A slow, steady pressure has been used in forcing the fluid into the subarachnoid space. It usually flows in without resistance if there has been a free flow from the needle previously. We have not used Quincke's funnel and tubing as recommended by Koplik,* but feel that perhaps it has certain advantages over the syringe.

During the injection of the first 15 cc., the majority of the patients complained of pain. It was very definitely associated with the process of injection itself. Whenever that was stopped the pain ceased—to begin again when pressure was applied to the piston. It was referred to the legs mostly, particularly the knees and the hips. Doubled up, with hips and knees flexed, they would beg to be allowed to "stretch" their legs. There was just as much pain with the legs extended, however. Case No. VI complained of pain about the rectum; whereas Case No. XII cried out each time the injection was resumed, "Let me sit on the chamber." Subsequent behavior suggested this was not a normal desire to defecate. Pain and hyperæsthesia persisted 18 hours in Case No. VI. Perhaps the cord itself was injured here. The irregular and rapid pulse in Case No. III was in keeping with the general condition after a long ride to the hospital, and was not dependent upon the injection. When primary chloroform anæsthesia was used, the squirming and struggling, present only during the injec-

* Loc. cit.

tion, pointed to discomfort in the legs. Consequent upon this, there was usually increased pulse and respiration. This experience taught the anæsthetist to always deepen the anæsthesia just before the injection. Case No. XXI, who suffered from the headaches, was complicated by hydrocephalus.

The following table contains quotations from the histories in regard to the disturbance *during the injection.*

TABLE No. VII.—DISTURBANCES ASSOCIATED WITH THE INJECTION OF SERUM.

| Number of case. | Number of tap. | Remarks. |
|---|---|---|
| II. | 2 | Cried for few hours. |
| III. | 1 | Pulse irregular—over 200 to minute. |
| | 2 | Pain in the knees. |
| | 3 | Pain in the knees. |
| | 4 | Pain in the knees. |
| | 5 | Pain in the knees. |
| | 6 | Pain in the knees. |
| V. | 1 | Cried out with pain. |
| VI. | 1 | Pain about the rectum. |
| | 2 | Very severe pain in hips and down legs for 18 hours; hyperæsthesia of legs; unable to move legs without great pain. |
| VII. | 1 | Struggled during injection. |
| VIII. | 1 | Pain referred to knees. |
| | 2 | Anæsthetized; from struggles, pain in legs. |
| IX. | 1 | Roused, disturbed; primary anæsthesia. |
| | 2 | Roused, disturbed; primary anæsthesia. |
| | 5 | Considerable distress; primary anæsthesia; squirmed and resisted. |
| X. | 1 | Considerable pain referred to knees. |
| XI. | 1 | Pain in back, legs, and feet. |
| | 2 | Pain in back, legs, and feet. |
| XII. | 1 | Cried out repeatedly, "Let me sit on chamber." |
| XIII. | 2 | Squirmed, groaned; from motion, pain in legs. |
| XIV. | 2 | Wriggled and cried. |
| | 4 | Cried out constantly. |
| XV. | 1 | Movements of legs suggesting pain. |
| XVI. | 1 | Crampy pain in hip and leg; wanted to stretch. |
| | 2 | Cramps in legs. |
| | 3 | Great pain in limbs. |
| XVII. | 2 | Squirmed and cried out. |
| XVIII. | 1 | Intense pain in knee joints; begged to stretch legs. |
| XXI. | 3 | Greatly upset; cried with pain in head for 4 hours. |
| | 4 | Tossed and screamed with pain; splitting headache. |

We might venture a remark as to the cause of this pain. Particular care was paid to warming the serum and keeping it warm until used. To the hand the fluid removed was never any warmer. We feel certain the pain is not due to cold serum, as Dunn * believes. The situation of the pain is in keeping anatomically with the idea that it is referred pain from the cord or cauda equina opposite the site of injection. It is not improbable that it is due to the pressure excited at that point just during the moment of injection.

6. AMOUNT INJECTED.—As the serum was obtained in 15 cc. bottles, and it was not desirable to keep it after being opened, the amounts injected were usually 15 cc. or multiples thereof. Dr. Flexner's suggestions were followed in most cases—to inject as much serum as spinal fluid removed, not exceeding 30 cc. In one instance Case No. XXI,

* Loc. cit.

45 cc. were injected at one time, and it seemed to cause the patient great discomfort for 12 to 18 hours. "He spent a miserable day, groaning and moaning with pain in head, neck, back and 'all over.' Neck stiff, head retracted, Kernig doubly positive, slight strabismus. In fact an intensification of all signs and symptoms."—(From the history.)

TABLE NO. VIII.—THE AMOUNT OF SERUM INJECTED.

| Case No. | Serum injected. | Fluid removed. | Day of disease. |
|---|---|---|---|
| I. | 15 | 15 | 58 |
| | 15 | 15 | 60 |
| II. | 25 | 35 | 48 |
| | 20 | 20 | 49 |
| | 20 | 20 | 51 |
| III. | 14 | 20 | 3 |
| | 30 | 40 | 5 |
| | 20 | 20 | 6 |
| | 25 | 46 | 9 |
| | 30 | 50 | 12 |
| | 30 | 60 | 16 |
| IV. | 15* | 12 | 14 |
| | 30* | 25 | 15 |
| V. | 30 | 40 | 22 |
| | 30 | 30 | 23 |
| | 15 | 62 | 24 |
| | 30 | 60 | 32 |
| VI. | 15 | 17 | 5 |
| | 15 | 16 | 6 |
| VII. | 30 | 30 | 1 |
| | 30 | 35 | 2 |
| | 15 | 49 | 2 |
| | 30 | 35 | 3 |
| | 15 | 30 | 3 |
| VIII. | 15 | 25 | 5 |
| | 15 | 15 | 6 |
| | 30 | 30 | 7 |
| IX. | 18 | 31 | 3 |
| | 15 | 24 | 4 |
| | 30 | 28 | 5 |
| | 15 | 15 | 7 |
| | 30 | 41 | 8 |
| | 30 | 45 | 10 |
| X. | 30* | 26 | 6 |
| XI. | 30 | 30 | 15 |
| | 15 | 16 | 16 |
| XII. | 30 | 34 | 3 |
| | 30 | 46 | 3 |
| XIII. | 30 | 31 | 4 |
| | 30 | 30 | 5 |
| | 30* | 19 | 5 |
| XIV. | 30* | 23 | 3 |
| | 30 | 30 | 4 |
| | 30 | 33 | 5 |
| | 15 | 21 | 6 |
| XV. | 30 | 30 | 3 |
| | 30 | 45 | 4 |
| XVI. | 15 | 18 | 7 |
| | 30* | 20 | 8 |
| | 30* | 12 | 9 |
| | 30 | 30 | 10 |
| XVII. | 15 | 24 | 7 |
| | 25 | 28 | 8 |
| XVIII. | 15 | 24 | 3 |
| | 30 | 65 | 4 |
| XIX. | 15* | 6 | 2 |
| | 30* | 18 | 2 |
| | 30* | 14 | 3 |
| XX. | 30 | 30 | 2 |
| | 15* | 5 | 3 |
| XXI. | 15 | 35 | 9 |
| | 30 | 65 | 10 |
| | 30 | 50 | 12 |
| | 30 | 35 | 13 |
| | 30 | 50 | 16 |
| | 45 | 50 | 19 |
| | 15 | 50 | 20 |
| | 15 | 40 | 40 |
| | 15 | 20 | 41 |
| | 30 | 35 | 42 |
| | 15 | 25 | 46 |
| XXII. | 30* | 2 | 6 |
| XXIII. | 10 | 20 | 8 |

* Denotes instances when the amount injected exceeded the amount removed.

In 12 instances more serum was injected than spinal fluid removed, and there was no intensification of the so-called pressure symptoms and signs. In fact, the patients seemed benefited. In Cases No. XVI and No. XVII the excess of serum amounted to 18 cc. In none of these cases was there the slightest disturbance attributable to this fact.

TABLE IX.—CASES WHERE MORE SERUM WAS INJECTED THAN SPINAL FLUID REMOVED.

| Case No. | Serum injected. | Fluid removed. | Excess serum. |
|---|---|---|---|
| IV. | 15 | 12 | 3 |
| | 30 | 25 | 5 |
| X. | 30 | 26 | 4 |
| XIII. | 30 | 19 | 11 |
| XIV. | 30 | 23 | 7 |
| XVI. | 30 | 20 | 10 |
| | 30 | 12 | 18 |
| XIX. | 15 | 6 | 9 |
| | 30 | 18 | 12 |
| | 30 | 14 | 16 |
| XX. | 15 | 5 | 10 |
| XXII. | 20 | 2 | 18 |

The amount of serum needed to produce results differed according to the cases. Experience soon taught us to inject as much as possible and as early as possible. In the severer cases tap and injection were done every 12 hours; whereas in the ordinary type, every 24 hours was sufficient. Reference to Table No. XI shows the largest amount of serum injected in any one case which recovered was 149 cc. in 6 injections.

Case No. IX received 138 cc. in 6 injections.
Case No. XVI received 120 cc. in 4 injections.
Case No. XIV received 105 cc. in 4 injections

The smallest amount to which any one case responded favorably was 10 cc. (No. XXIII). Three cases received but 1 injection, 10, 20 and 30 cc., respectively. In 11 cases the spinal fluid was found sterile at the second puncture, that is after one injection of serum. The serum was given, however, at intervals of 12 to 24 hours until the responsive reaction in temperature, symptoms, and signs was obtained. To obtain this it was necessary usually to give one or two injections after that one which rendered the fluid sterile. Perhaps the first injection might have been all that was necessary, and the following one or two may have been given in a period of convalescence which would have proceeded without them. But the extra injections clinched the recovery, as it were, and it seems must have hastened the clearing with their antitoxic influence. The first injection shows by rendering the spinal fluid sterile in so many cases that it is mainly bactericidal in effect. If the organisms are abundant, the liberation of endotoxin is great, and the additional serum in neutralizing this remedies the temporary harm intentionally brought about by the killing of the organisms.

7. Other Applications of the Serum.—It is in just such instances as these, in which the toxæmia is apparently increased by the bactericidal influence of the first injection, that the *subcutaneous* application of the serum may be of value. The serum is applied locally in the subarachnoid space or in a joint, because it must be in a certain concentration to kill the diplococci. But the toxins are in the general circulation and there, by subcutaneous administration, we apply the antitoxin. It seems probable that a combination of the subcutaneous and subarachnoid applications is the best procedure in the case of a severe infection.

And one step further must be taken in the extremely sthenic cases. In this type nearly always purulent exudate and organisms are found in the lateral cerebral ventricles at autopsy. Seven of 15 autopsies of this disease in the Pathological Department of the Johns Hopkins Hospital note findings of this character, namely, "fourth ventricle, central canal, and lateral ventricles dilated and contain turbid fluid; fibrino-purulent exudate on the ependyma." This is not only a factor in closing the meshwork between the subarachnoid and intraventricular spaces, but furthermore provides a good habitat for the organisms—where they persisted over four months in one case[25] in this clinic. In adults, as Cushing has pointed out, a buttonhole must first be made by the surgeon (see Keen's Surgery for point of election). Once made, the ventricle can be tapped at will. In children, the needle can be passed in the sutures or fontanelle. It will be imperative, we feel, to administer serum by this route in certain cases in order to remove such a menacing condition.

Other local foci, metastatic or part of a general infection, can be treated effectually by direct application of the serum. The case of purulent arthritis reported by Ladd * was cured by injection of the serum directly into the joint after diplococci had been demonstrated in the pus aspirated from it.

8. Anæsthesia.—Various methods of anæsthesia were employed. We preferred no anæsthetic at all, local or general, when it was possible. If the patient was quiet and it seemed likely he would stand it, either no anæsthetic was used or simply Schleich's solution locally to anæsthetize the skin. These were the patients who complained during the injection. A noisy, delirious, struggling patient was given primary chloroform. This was used also in convalescence when the patients were more normal, more likely to be frightened and to resist. Our thanks are due to Dr. Gatch, anæsthetist of the surgical staff, for his skilful services. He was able to keep the patients under the lightest anæsthesia, allowing satisfactory puncture and injection, but not sufficient to upset the general condition. It was his observation that the pulse and respirations were changed as a zero pressure was approached in removing fluid, and it was usually his warning which stopped the removal, inasmuch as it is very tempting to continue as long as the fluid is dropping freely. He learned from experience to deepen the anæsthesia just before the injection was begun, and so to avoid the pain and struggling incidental to it.

* Loc. cit.

9. Indications for Serum.—Before the positive diagnosis was made, there was no hesitation to puncture any case *suspected* of being *meningitis,* or to inject serum whenever there was a *suspicion* of it being the *epidemic type.* The same preparation was always made as for cases positively diagnosed. Even when the fluid was not cloudy, cloudiness seeming to be the indication in many clinics, serum was injected. Case No. II was our lesson in this. Here the fluid was under 400+ mm. pressure, was clear and limpid, containing flocculi, and showed a cell count of small mononuclear leucocytes amounting to 62 per cent and polymorphonuclears 38 per cent. It was considered a tuberculous fluid and no serum injected. Cultures yielded the diplococcus and the next specimen was very cloudy with polymorphonuclears. On the other hand, a fluid clouded with polymorphonuclear leucocytes, plus a general leucocytosis, was found in one case of tuberculous meningitis.

However, no mistake can be made in giving the serum. It is well demonstrated that no harm can be done to cases not of the epidemic type. In fact, some benefit is possible. By this procedure, serum was given to the following diseases (Table No. X) which were of doubtful diagnosis and exhibited signs or symptoms suggesting the possibility of epidemic meningitis. None of them were apparently influenced a particle in general condition or in the course of the disease. The cell content of the spinal fluid and the leucocytes in the circulating fluid were affected in a remarkable way (see Section V).

Table No. X.—Other Infections Which Received Intraspinal Serum on Suspicion.

| | |
|---|---|
| Tuberculous meningitis | 7 cases. |
| Pneumococcal meningitis | 3 " |
| Influenzal meningitis | 1 " |
| Subacute endocarditis | 1 " |
| Acute broncho-pneumonia | 1 " |
| Cholera infantum | 1 " |
| Typhoid fever | 2 " |
| Total | 16 cases. |

As indication for the second injection of serum, on the other hand, we required something positive to be found in the specimen of fluid obtained at the first puncture. Either a demonstration of the diplococci in smears or their recovery by culture was demanded.

10. Serum Disease and Anaphylaxis.—Only two cases developed urticarial eruptions after receiving serum, and in both the amount

injected was 75 cc. Two cases exhibited erythematous blotches over the cheeks and ears. Sudden, transitory, and localized œdema occurred in two cases. The toxic arthritis in Case No. XVI appeared after the injection of 90 cc. of serum. This arthritis was probably not related to the serum, however. The skin specialists considered the vesicular eruptions in Case No. II as due to the serum, the erythema in Case No. XVII as independent of it.

Sixteen of the 23 cases gave no manifestation of serum disease.

TABLE No. XI.—EVIDENCES OF SERUM DISEASE.

| Case No. | Serum. cc. | Day of disease. | Total amt. cc. | Evidence of serum disease. |
|---|---|---|---|---|
| I. | 15<br>15 | 58<br>60 | 30 | Negative. |
| II. | 25<br>20<br>20 | 48<br>49<br>50 | 65 | On 52d day, vesicular eruption over thighs and legs; small, discrete vesicles which soon became infected. Crust and brown stain on discharge. Attributed to serum by Dr. Lord. |
| III. | 14<br>30<br>20<br>25<br>30<br>30 | 3<br>5<br>6<br>9<br>13<br>16 | 149 | 14th day, flush of left cheek and right ear; slight œdema; ear blistered (frostbite?). |
| IV. | 15<br>30 | 14<br>15 | 45 | Negative. |
| V | 30<br>30<br>15<br>30 | 22<br>23<br>24<br>32 | 105 | From 25th to 30th days, flushes over left cheek and ear; urticarial wheals on trunk and limbs. |
| VI. | 15<br>15 | 5<br>6 | 30 | Negative. |
| VII. | 30<br>30<br>15<br>30<br>15 | 1<br>2<br>2<br>3<br>3 | 120 | Negative. |
| VIII. | 15<br>15<br>30 | 5<br>6<br>7 | 60 | Negative. |
| IX. | 18<br>15<br>30<br>15<br>30<br>30 | 3<br>4<br>5<br>7<br>8<br>10 | 138 | Negative. |
| X. | 30 | 6 | 30 | Negative. |
| XI. | 30<br>15 | 15<br>16 | 45 | Negative. |
| XII. | 30<br>30 | 3<br>3 | 60 | Negative. |
| XIII. | 30<br>30<br>30 | 4<br>5<br>5 | 90 | Negative. |

TABLE NO. XI.—EVIDENCES OF SERUM DISEASE—Continued.

| Case No. | Serum. cc. | Day of disease. | Total amt. cc. | Evidence of serum disease. |
|---|---|---|---|---|
| XIV. | 30 | 3 | 105 | 8th day, sudden, transitory œdema of face, hands, forearms, and eyelids; not of feet or ankles. |
| | 30 | 4 | | |
| | 30 | 5 | | |
| | 15 | 6 | | Urine: Trace of albumen due to a few leucocytes. |
| XV. | 30 | 2 | 60 | Negative. |
| | 30 | 3 | | |
| XVI. | 30 | 7 | 120 | 10th day, puffiness over wrists, tenderness, limited motion; arthritis before onset; "toxic arthritis." |
| | 30 | 8 | | |
| | 30 | 9 | | |
| | 30 | 10 | | |
| XVII. | 15 | 7 | 40 | 18th day, day after empyema drainage, erythematous blotches over chest; erythema multiforme (Dr. Gilchrist). |
| | 25 | 8 | | |
| XVIII. | 15 | 3 | 45 | Negative. |
| | 30 | 4 | | |
| XIX. | 15 | 2 | 75 | 7th day, profuse urticarial eruption. |
| | 30 | 3 | | |
| | 30 | 3 | | |
| XX. | 30 | 2 | 45 | Negative. |
| | 15 | 3 | | |
| XXI. | 15 | on 5 days | 270 | (Spread out: On 9th, 10th, 12th, 13th, 16th, 19th, 20th, 27th, 40th, 41st, 42d, and 46th days.) |
| | 30 | on 6 days | | |
| | 45 | on 1 day | | Negative. |
| XXII. | 20 | 6 | 20 | Negative. |
| XXIII. | 10 | 8 | 10 | Negative. |

There was no opportunity of considering anaphylaxis further in this series. The above table shows the longest intervals between injections to have been 13 and 7 days in Case No. XXI, 10 days in Case No. XVI, and 8 days in Case No. V.

In Case No. V only was there anything resembling a reaction of hypersensibility. The temperature rose to 102.6° F. in 4 hours, and fell as rapidly. The child became sleepless and irritable, the neck a little stiff, and a strabismus appeared. This sounds like a reappearance of the original signs of the meningitis. The other cases were treated at intervals of from 12 hours to 4 days.

### III. ACCESSORY TREATMENT.

In addition to the serum, a general line of treatment was followed, which was both supporting and eliminating. This same plan, plus repeated lumbar punctures but minus the serum, of course, is what was followed in the previous 19 years. So the conditions were the same in both series, except for the addition of serum to the 1908 cases.

1. Isolation.—The cases were segregated upon the isolation ward, where they occupied rooms of their own. Their bed-linen, dishes, urinals, and bedpans were isolated, and the disinfection of these, as well as of the excreta, was cared for according to our routine for contagious diseases. The patients, and those in attendance upon them, were given nose and throat sprays and irrigation.

2. Nourishment.—The diet given during the acute illness amounted to liquids—hot broths, milk, albumen, cocoa or well-diluted coffee. As soon as they would take it, soft eggs and toast and cereals were added, and no time was wasted in convalescence to restore their strength with a liberal diet, milk, and raw eggs. Nearly every case received whiskey every 3 or 4 hours during the febrile period, from ℥ii to ℥i, according to the age and the degree of toxæmia. In the children particularly, it was oxidized readily and was considered in the light of a useful food.

In Cases Nos. IV, VII, and XIII, all fatal, gavage and rectal feeding were employed.

3. Hydrotherapy.—Both internal and external hydrotherapy were made use of. Water by mouth was forced by the nurses—4-ounce feeders every half hour, day and night, when awake. This has produced an excretion of 3 to 4 litres of urine on the average. In addition, while the temperature was high, it was our custom to order salt solution per rectum, in some cases by the continuous-drop method, 50-75 cc. an hour; in others by the high-rectal injection of 150-400 cc. every 4 hours. Ice-water sponges, ice packs, and tubs were used. Warm tubs seemed to relieve the pain and rigidity in some cases; whereas tubs at 70-80° F. were used to combat hyperpyrexia.

As much as we believe in hydrotherapy, we feel forced to call attention to the fact that every one of the three cases to receive cold tubs developed pulmonary complications, to wit, bronchopneumonia in Cases Nos. XIV and XVII, and acute fibrinous pleurisy in Case No. IX.

4. Medicines.—It was the exception to need any drugs. Such stimulants as strychnia, digitalis, digitaline, digalen, and camphor were only occasionally indicated. Morphia, atropine, and chloroform helped to control the convulsions. Coffee was added to the salt solution per rectum in some cases.

### IV. The Cases before Treatment with Serum.

The histories of these cases, their symptoms, and the signs exhibited convince us that in every instance of the survivors the course of the disease was modified by the serum. Even in the 4 fatal cases, as we shall show later, there was an encouraging effect produced.

1. Character of Cases.—The first two cases in the series were chronic, receiving serum first on the fifty-eighth and forty-eighth days, respectively. They responded rapidly and both recovered without sequelæ. Though neither of these cases was extremely ill, they both were losing ground, and it seems remarkable that a perfect cure should have been accomplished in so short a time—a cure of a process which had been allowed to go so long.

Table No. XII.—Type of Cases and Age of Patients.

| Case No. | Age. | Acute. | | | | Chronic. | Result. |
|---|---|---|---|---|---|---|---|
| | | Mild. | Severe. | Very severe. | Fulminant. | | |
| I. | 36 yrs. | | | | | + | R.* |
| II. | 6 " | | | | | + | R. |
| III. | 15 " | | | + | | | R. |
| IV. | 29 mos. | | | + | | | D.* |
| V. | 13 " | | | + | | | R. |
| VI. | 23 yrs. | | + | | | | R. |
| VII. | 27 " | | | | + | | D. |
| VIII. | 5 " | | + | | | | R. |
| IX. | 5 " | | | + | | | R. |
| X. | 7 " | + | | | | | R. |
| XI. | 7 " | | + | | | | R. |
| XII. | 7 " | | + | | | | R. |
| XIII. | 25 " | | | + | | | D. |
| XIV. | 9 " | | | + | | | R. |
| XV. | 11 " | | + | | | | R. |
| XVI. | 27 " | | + | | | | R. |
| XVII. | 25 mos. | | | + | | | R. |
| XVIII. | 30 yrs. | + | | | | | R. |
| XIX. | 6 " | | + | | | | R. |
| XX. | 15 " | | + | | | | R. |
| XXI. | 27 " | | | + | | | D. |
| XXII. | 27 " | + | | | | | R. |
| XXIII. | 17 " | + | | | | | R. |
| Total | | 4 | 8 | 8 | 1 | 2 | |

* R recovered; D died.

The other 21 cases were reached in the acute attack. Case No. VII we have classed as *fulminant.* He was unconscious from the onset and suffering convulsions continually. He was considered hopeless, but prolonged efforts were used to give the serum at least 3 days in which to produce some effect. He died on the fourth day.

The other 3 fatal cases were *very severe* infections at the outset. Death is attributable to consequent hydrocephalus in Case No. XXI; to complicating adiposis, myocarditis, and pneumonia, in Case No. XIII; and to the fact that serum was given *too late* to be serviceable in Case No. IV.

The remaining 5 cases classed as *very severe* were extremely so, and nothing but a very doubtful prognosis was given in each instance. The outlook in two of them was gloomy on account of complications.

The 8 *moderately severe* attacks gave no manifestations which suggested probable, or even possible, recovery without the use of the serum. In each case the disease was outspoken and active.

Four cases were *mild* enough to allow the possibility of their clearing spontaneously. Petechial eruptions, which some take as a measure of severity, were present in 7 cases (Nos. III, VI, VIII, XIII, XIV, XV, and XXI). Four of these were "very severe" cases, and the other three "severe."

2. Day of Disease.—The day of the disease on which the patient first receives serum will depend in the future upon the ability and intelligence of the local physician. It is a powerful factor in determining the course and outcome of the attack.

Table No. XIII.—Table Showing Day of First Injection.

| Case No. | Day of first injection. 1st | 2d | 3d–7th | 8th–21st | 22d– | |
|---|---|---|---|---|---|---|
| I. | | | | | 58 | Recovery. |
| II. | | | | | 48 | Recovery. |
| III. | | | 3 | | | Recovery. |
| IV. | | | | 14 | | Fatal. |
| V. | | | | | 22 | Blind before serum. |
| VI. | | | 5 | | | Recovery. |
| VII. | 1 | | | | | Fatal; fulminant. |
| VIII. | | | 5 | | | Recovery. |
| IX. | | | 3 | | | Recovery. |
| X. | | | 6 | | | Recovery. |

TABLE No. XIII.—TABLE SHOWING DAY OF FIRST INJECTION—Continued.

| Case No. | Day of first injection. 1st | 2d | 3d–7th | 8th–21st | 22d– | |
|---|---|---|---|---|---|---|
| XI. | | | | | 15 | Recovery. |
| XII. | | | 3 | | | Recovery. |
| XIII. | | | 4 | | | Fatal; complications. |
| XIV. | | | 3 | | | Recovery. |
| XV. | | 2 | | | | Recovery. |
| XVI. | | | 7 | | | Recovery. |
| XVII. | | | 7 | | | Recovery. |
| XVIII. | | | 3 | | | Recovery. |
| XIX. | | 2 | | | | Recovery. |
| XX. | | 2 | | | | Recovery. |
| XXI. | | | | 9 | | Fatal; hydrocephalus. |
| XXII. | | | 6 | | | Recovery. |
| XXIII. | | | | 8 | | Recovery. |
| Total cases | 1 | 3 | 12 | 3 | 4 | |
| | | 16 | | | | |

In this series, 16 out of 23 were admitted in the first week; 3 in the second; and 4 after the second week. One of these 4, in the third week or thereafter, suffered greatly, we feel, on this score. Case No. V was already blind when admitted on the twenty-second day. Case No. IV, treated first on the fourteenth day, was beyond the reach of succor when admitted. Case No. IX died much later of hydrocephalus, but serum earlier than the ninth day might have prevented this disastrous sequel. We feel, of course, that the sooner the serum is applied, the better the result. The only case in the first day column was the fulminant one, No. VII. The 3 second-day cases (Nos. XV, XIX, and XX), severe on admission (see Table XII), all responded rapidly to serum and ran a mild course.

Besides the fulminant case, there was one other to die which received serum in the first week. It was Case No. XIII, treated first on the fourth day—the fat, colored woman with myocarditis and bronchopneumonia. The table bears out the statement as to the greater efficacy of early serum.

3. AGE, COLOR, AND SEX.—In this series the absence of cases under one year of age detracts interest in regard to age. The one case under two years of age recovered. The interesting group is that over

20 years. Of 8 cases, 3 died. Compare the group of 8 cases between 5 and 10 years of age, with no deaths. We believe that adults of 20 years and over are not "less subject to the beneficial action of the serum than younger persons." But from our experience with Case No. XIII alone, we are impressed with the fact that men and women of these ages are apt to have their heart muscles, arteries, and kidneys in no suitable condition to stand the strain incidental even in the use of the serum. Complications like pneumonia are more apt to develop and carry them off.

TABLE NO. XIV.—AGES OF THE PATIENTS.

| Age. | Cases. | Recovered. | Died. |
|---|---|---|---|
| Under 1 year | 0 cases | 0 | 0 |
| Between 1 and 2 years. | 1 case (V) | 1 | 0 |
| " 2 " 5 " | 2 cases (IV, XVII) | 1 | 1 |
| " 5 " 10 " | 8 cases (II, VIII, IX, X, XI, XII, XIV, XIX) | 8 | 0 |
| " 10 " 20 " | 4 cases (III, XV, XX, XXIII) | 4 | 0 |
| Over 20 years | 8 cases (I, VI, VII, XIII, XVI, XVIII, XXI, XXII) | 5 | 3 |

In this small series, as in the larger one of Flexner's * analysis, the best prognosis is in the group between 5 and 10 years of age.

As the table shows, only 6 of the patients were of the colored race—2 females and 4 males. One of the females died—an adult.

Of the 17 whites, only 3 were females. The 3 fatal cases were all males—1 child and 2 adults.

TABLE NO. XV.—COLOR AND SEX.

| | White. | Black. | Total. |
|---|---|---|---|
| Male | 14 | 4 | 18 |
| Female | 3 | 2 | 5 |
| | 17 | 6 | 23 |

The series, of course, is too small to allow deductions in this regard.

4. SYMPTOMS.—The onset was sudden in every case, as a rule out of a clear sky.

(1) *Predisposing causes* were apparent in a few cases, as follows:

(a) An attack of *influenza* of 2½ to 3 weeks' duration preceded in Cases Nos. III, V, and VI.

(b) *Trauma* was emphasized by the parents in 2 cases, which may have been a factor in producing a *locus minoris resistentiæ*. Case No. XVII fell the day before and struck her head on a couch, severe

* Loc. cit.

nosebleed following. Case No. XIX, 5 hours previous, fell off the front steps and struck his head "a solid crack."

(c) *Alcohol.*—Case No. VII had been on a protracted spree.

(d) *Acute Arthritis.*—Case No. XVI was suffering from an attack of acute polyarthritis at the time.

(e) *Chronic Nephritis.*—Case No. XXIII had œdema of the eyelids, albuminuria, and cylindruria, and it is a question if her convulsions were not uræmic.

Only 2 cases gave history of contact immediate or indirect with the disease.

Case No. VII lost his child 2 months previously from "meningitis."

Case No. XV was taken ill 48 hours after his sister (No. XIV).

(2) *Prodromal symptoms* were rare: Peevishness for 12 hours, Case No. VIII; giddiness, Case No. IX; abdominal pain, Case No. XIII.

Thirteen of the 23 cases were apparently in their ordinary state of health when attacked with the disease. The onset, as stated, was sudden in all instances. Three cases were asleep when the first symptoms appeared. Vomiting ushered in two of these, Cases Nos. V and XIX, children, and convulsions the third, Case No. VII, an adult. Cases Nos. IX and XI, children, were sent home from school on account of headache, vomiting and fever. Case No. III had such a severe headache he stopped work at noon.

TABLE No. XVI.—SYMPTOMS OF ONSET.

| | Vomiting. | Headache. | Chill and Fever. | Fever. | Pains. | Malaise. | Convulsions. | Cases. |
|---|---|---|---|---|---|---|---|---|
| Vomiting | IV, V, IX, XVII, XIX. | XIV, XV, I, II, X. | I. | II. | X, XVI. | XVI. | | 11 |
| Headache | XIV, XV, I, II, X. | III, VI. | XII, I. | XI, II. | VIII, X. | | | 10 |
| Chill and Fever. | I. | XII, I. | XIII, XXI. | | | XX. | | 5 |
| Fever | II. | XI, II. | | XXIII. | | | | 3 |
| Pains | X, XVI. | VIII, X. | | | XVIII. | XVI. | | 4 |
| Malaise | | | | | | XX, XXII, XVI. | | 3 |
| Convulsions | | | | | | | VII. | 1 |

(3) The *symptoms of onset* were very similar in all cases:

(a) *Vomiting* was the commonest initial manifestation. It occurred in 11 cases:

Alone in 5 (IV, V, IX, XVII and XIX).
With headache in 2 (XIV and XV).
With headache, chill and fever in 1 (I).
With fever and headache in 1 (II).
With headache and pain in the back and stomach in 1 (X).
With general discomfort, and pain and stiffness in the neck in 1 (XVI).

(b) *Headache* occurred in 10 cases:

Alone in 2 cases (III and VI).
With pain in legs in 1 (VIII).
With fever in 1 (XI).
With chill and fever in 1 (XII).
With vomiting in 2 (XIV and XV).
With chill, fever and vomiting in 1 (I).
With fever and vomiting in 1 (II).
With vomiting and pain in back and stomach in 1 (X).

The headache was usually frontal and very severe. The patients declared it would drive them crazy.

(c) *Chill and fever* occurred in 5 cases:

Alone in 2 (XIII and XXI).
With headache in 1 (XII).
With drowsiness in 1 (XX).
With headache and vomiting in 1 (I).

(d) *Pains* occurred in 4 cases:

In the head, neck, chest, back and legs, stabbing and periodic in character in 1 (XVIII).
In the legs, with headache in 1 (VIII).
In the back and stomach with headache and vomiting in 1 (X).
In the neck (plus stiffness), with vomiting and general discomfort in 1 (XVI).

(e) *Fever* occurred in 3 cases:

Alone in 1 (XXIII).
With headache in 1 (XI).
With headache and vomiting in 1 (II).

(f) *General malaise* occurred in 3 cases:

With drowsiness in 2 (XX and XXII).
With general discomfort in 1 (XVI).

(g) *Convulsions* marked the onset of 1 case (No. VII).

(4) *Symptoms After Onset and Before Serum.*—The interval between onset and the first injection of serum has varied from 24 hours to 58 days (see Table No. XII). The majority have received serum in the first week. In this interval more or less the same clinical picture has developed.

TABLE NO. XVII.—SYMPTOMS DEVELOPING BETWEEN ONSET AND FIRST INJECTION OF SERUM.

| Case No. | Chills. | Fever. | Delirium. | Headache. | Vomiting. | Pain in neck. | Hyperæsthesia. | Convulsions. | Unconsciousness. | Miscellaneous. |
|---|---|---|---|---|---|---|---|---|---|---|
| I. | + | + | + | + | | | + | | | In paroxysms. |
| II. | | +* | | + | | | + | | | Cephalic cry. |
| III. | | + | + | | | | + | + | | |
| IV. | | + | | + | | | | + | + | Restlessness. |
| V. | | + | | | | | + | + | | Prostration. |
| VI. | | + | + | | + | | | | | Inability to swallow. |
| VII. | | + | | | | | | | + | |
| VIII. | | + | | | + | | | | | |
| IX. | | + | + | | | | | | | Stupor. |
| X. | | + | + | | | | | | | |
| XI. | | (2) | + | | + | + | | | | |
| XII. | | (2) | | | + | + | | + | | |
| XIII. | | (2) | | + | | + | | | | Restlessness. |
| XIV. | | + | + | | | | | | | |
| XV. | | + | + | | | | + | | | |
| XVI. | | (2) | | + | | | | + | + | |
| XVII. | | + | | + | | | + | | | Stupor. |
| XVIII. | | + | | | + | | | | | Walked into hospital |
| XIX. | | + | + | + | | | | + | | Involuntary stools and urine. |
| XX. | | (2) | + | | + | | | | | |
| XXI. | + | + | | + | | | + | | | Walked into hospital. |
| XXII. | + | + | | + | | | + | | | Prostration. |
| XXIII. | | (2) | + | | | | | + | + | |
| Cases. | 3 | 23 | 11 | 9 | 6 | 3 | 8 | 7 | 4 | |

* Intermittent. (2) From onset.

The symptoms, as the tables show, form in total but a very small group. On analysis, they consist of:

(a) *Chills.*—Repeated chills occurred in 3 cases. In Case No. I they initiated recurring paroxysms of fever, delirium, headache, and general sensitiveness and pains. In Cases Nos. XXI and XXII they recurred daily, with rises in temperature. It was noted above that 3 other cases had a chill at onset.

(b) *Fever.*—Every case developed fever, 6 at onset, and the rest very rapidly after onset. Nothing can be said about the type of fever before admission to the ward, except in a few instances. Case No. I had 6 paroxysms, as described above, in 56 days. The fever in Case No. II became intermittent in type, with morning fall and evening rise, and an intensification of frontal headache and hyperæsthesia during the elevations. The paroxysm would last 18 hours, the maximum temperature being 105° F. This condition persisted 4 weeks.

This intermittent type of fever interested us very much in Case No. XVI, in which it was the form of temperature with daily chills occurring in a relapse. It suggested a complication rather than a recrudescence. Moeller [26] reports a somewhat similar case.

The fever was high in the majority of cases, 99 to 106° F. as is evidenced by its association with:

(c) *Delirium* in 11 cases. The majority were of a wild, noisy type, necessitating restraint. In Case No. XV it is described as a low, muttering delirium. It was not a feature of onset in any case.

(d) *Headache* in 9 cases. It was usually frontal, very severe, and bitterly complained of. Eight other cases had it at the onset.

(e) *Vomiting* developed in 6 cases, in addition to the 11 in which it featured at the onset. In only Case No. I was nausea associated. In Case No. X, pain in the stomach preceded the vomiting.

(f) *General hyperæsthesia and pains over the body* occurred in 8 cases, whereas in 4 others the pains and soreness were localized *in the neck.* In 2 other cases they marked the onset.

(g) *Unconsciousness.*—Four cases were unconscious when brought into the hospital.

(h) *Convulsions* occurred in 7 cases. In another case they began at onset and continued. They were clonic in all 8 cases, involving the whole body in 6, the right half in 1, and the left in 1. They occurred 3 times in 3 cases, twice in 1, once in 1, and repeatedly in 3 cases.

In addition the cephalic cry, stupor, prostration, restlessness, inability to swallow, and loss of control of the sphincters were part of the picture.

Two of the cases walked into the hospital supported by relatives, one of these irrational at the time. The other 21 were brought in on stretchers.

Some of the symptoms of onset persisted, and they should be combined with the symptoms developing after onset in order to truly show the relative frequency of the individual symptoms.

TABLE NO. XVIII.—SYMPTOMS PERSISTING FROM ONSET AND DEVELOPING AFTER ONSET.

| | Chill or chills. | Fever. | Delirium. | Headache. | Vomiting. | Pain in neck. | Hyperæsthesia. | Convulsions. | Unconsciousness. | Indisposition, stupor, etc. |
|---|---|---|---|---|---|---|---|---|---|---|
| Persisting from onset | 2 | 6 | 0 | 9 | 0 | 1 | 0 | 1 | 1 | 1 |
| Developing betw. onset and serum injection | 1 | 17 | 11 | 7 | 6 | 3 | 7 | 7 | 2 | 8 |
| Total | 3 | 23 | 11 | 16 | 6 | 4 | 7 | 8 | 3 | 9 |

5. SIGNS.—The signs indicative of meningitis are less numerous than the symptoms in these cases. No division can be made of the signs into those before admission and those after, inasmuch as no uniform observations were made before arrival upon the ward. However, it is fair to assume, in the absence of improvement, that most of the signs persisted and were recorded on admission. At any rate the following signs were present on the ward before the administration of serum.

TABLE NO. XIX.—SIGNS BEFORE SERUM.

| Case No. | Stiffness of neck. | Retracted head. | Arched back. | Kernig sign. | Strabismus. | Herpes. | Petechial eruption. | Miscellaneous. |
|---|---|---|---|---|---|---|---|---|
| I. | + | + | + | | | | | Nystagmus; coarse tremor. |
| II. | + | + | + | + | | | | Cephalic cry. |
| III. | + | + | + | + | | | + | Rigidity of limbs. |
| IV. | + | − | | neg. | | | | Rigidity of limbs. |
| V. | + | + | | neg. | | | | Paresis of rt. side; blindness. |
| VI. | + | + | | + | | | + | Unequal pupils. |
| VII. | + | + | + | + | divergent | + | | Paralysis of rt. side. |
| VIII. | + | + | + | + | | | + | |
| IX. | + | + | | − | | | | |
| X. | + | | | + | | − | | |
| XI. | + | − | + | + | convergent | + | | |
| XII. | + | | | + | | | | Abdom. reflexes absent. |
| XIII. | + | | | + | divergent | | + | Constant jerking. |
| XIV. | + | − | | + | convergent | | + | Abdom. reflexes absent. |
| XV. | + | | | + | | | + | |
| XVI. | + | − | | + | convergent | | + | Acute arthritis. |
| XVII. | − | | | neg. | divergent | + | | |
| XVIII. | + | | | + | | | | |
| XIX. | − | | | neg. | divergent | | | |
| XX. | − | | | neg. | convergent | | | |
| XXI. | − | | | + | | | + | |
| XXII. | − | − | | + | | | | |
| XXIII. | | | | neg. | divergent | | | (Edema; albuminuria; cylindruria. |
| Total: | 22 | 13 | 6 | 16 | 9 | 4 | 8 | |

(a) *Stiffness of the neck* was present in 22 out of 23 cases—the most constant and reliable of signs. As a rule, with the hand under the occiput, the head and trunk could be lifted without flexion of the neck. Attempts at passive motion always caused pain and resistance.

(b) *Retraction of the head* is the next degree of rigidity, and was present in 13 cases.

(c) *Arching of the back* might be called the third degree, and was present in only 6 cases. These last two signs made the prone position painful and avoided.

(d) *The Kernig sign* was interpreted as the physical impossibility to extend the leg when the thigh was flexed upon the abdomen. It was positive in 16 of the 23 cases. No note was made in regard to it in Case No. I. It was negative in 6 cases. Its relation to age interests us. The ages of the negative cases are:

| | | |
|---|---|---|
| Case No. | IV | 29 months. |
| Case No. | V | 13 months. |
| Case No. | XVII | 25 months. |
| Case No. | XIX | 6 years. |
| Case No. | XX | 15 years. |
| Case No. | XXIII | 17 years. |

Two-thirds of the negative cases were under 12 years of age. The following table shows the relation of age and occurrence of the Kernig sign:

TABLE NO. XX.—RELATION OF AGE AND OCCURRENCE OF KERNIG SIGN.

| Age. | Cases. | Kernig sign. | |
|---|---|---|---|
| | | Positive. | Negative. |
| Under 1 year | 0 | 0 | 0 |
| Between 1 and 2 years | 1 | 0 | 1 |
| " 2 " 5 " | 2 | 0 | 2 |
| " 5 " 10 " | 8 | 7 | 1 |
| " 10 " 20 " | 4 | 2 | 2 |
| " 20 " 40 " | 8 | 8 | 0 |

Only 3 cases in the series were under 5 years of age and none of them had a positive Kernig sign at any time.

(e) *Strabismus.*—Paresis of an external muscle of the eyes occurred in 9 cases. The resulting squint was divergent in 5 cases, convergent in 4. In 2 more cases it appeared during convalescence, convergent in Case No. II, divergent in Case No. III. In Case No. XI it was still present upon discharge, but cleared up in all the other cases.

(f) *Herpes* was present in only 5 of the cases on admission, but

developed in 4 more in the first 3 days upon the ward. It was labial in type in all 9 cases, and associated with herpes nasalis in one of these.

(g) *Petechial eruption* was present in 8 cases, all of them severe. In 6 it was over the chest, abdomen, back, arms, and legs; in 2 simply upon the abdominal wall. In none of them was it localized about the joints.

(h) The abdominal reflexes were absent in Cases Nos. XII and XIV. Case No. V had paresis of the right arm and leg, and Case No. VII paralysis of the entire right side, flaccid, with absent reflexes and positive Babinski. The unequal pupils were conspicuous in Case No. VI. Case No. I had lateral nystagmus and a coarse tremor. Case No. V was blind upon admission. Case No. XVI had an acute polyarthritis, and No. XXIII, œdema, albuminuria, and cylindruria.

6. The Blood.—Every one of the cases showed an outspoken leucocytosis before the administration of serum. (The leucocytes before serum was given were not recorded in 2 cases. Case No. I was observed by another service. In Case No. XVIII the record was mislaid.) The lowest count was 12,080, in Case No. XVI; the highest, 45,000, in Case No. IV. The average for the 21 cases was 29,688, practically 30,000. Only 4 had counts less than 20,000. The rest (17) were between 20,000 and 45,000. Eleven cases had counts over 30,000.

Table No. XXI.—Leucocytosis before Serum.

| Case No. | 10,000–20,000 | 20,000–30,000 | 30,000–40,000 | 40,000–50,000 |
|---|---|---|---|---|
| I. | (?) | | | |
| II. | | | 30,000 | |
| III. | | 24,000 | | |
| IV. | | | | 45,000 |
| V. | | | | 40,800 |
| VI. | | 24,000 | | |
| VII. | | 24,000 | | |
| VIII. | | 23,400 | | |
| IX. | | | 30,000 | |
| X. | | 26,800 | | |
| XI. | 16,400 | | | |
| XII. | | | | 43,400 |
| XIII. | | | 36,080 | |
| XIV. | | | 32,600 | |
| XV. | | | | 40,600 |
| XVI. | 12,080 | | | |
| XVII. | | | | 40,400 |

TABLE NO. XXI.—LEUCOCYTOSIS BEFORE SERUM—Continued.

| Case No. | 10,000–20,000 | 20,000–30,000 | 30,000–40,000 | 40,000–50,000 |
|---|---|---|---|---|
| XVIII. | (?) | | | |
| XIX. | | | 35,600 | |
| XX. | | | | 44,000 |
| XXI. | 13,000 | | | |
| XXII. | 16,300 | | | |
| XXIII. | | 25,000 | | |
| Total. | 4 | 6 | 5 | 6 |

The fresh blood was always examined and an approximate idea gained therefrom of the predominating white-blood corpuscle. In every case it was the polymorphonuclear neutrophilic leucocyte. In Case No. II, 78 per cent of 30,000 white-blood corpuscles were polymorphonuclear leucocytes, and the rule was both an absolute and relative increase in this type of cell.

As the following table shows, the day of the disease apparently had nothing to do with the degree of leucocytosis.

TABLE NO XXII.—LEUCOCYTE COUNTS CLASSIFIED ACCORDING TO DAY OF DISEASE.

| Case No. | 1st day. | 2d day. | 3d–7th day. | 2d week. | 3d week on. |
|---|---|---|---|---|---|
| I. | | | | | (?) |
| II. | | | | | 30,000 |
| III. | | | 24,000 | | |
| IV. | | | | 45,000 | |
| V. | | | | | 40,800 |
| VI. | | | 24,000 | | |
| VII. | 24,000 | | | | |
| VIII. | | | 23,400 | | |
| IX. | | | 30,000 | | |
| X. | | | 26,800 | | |
| XI. | | | | | 16,400 |
| XII. | | | 43,400 | | |
| XIII. | | | 36,080 | | |
| XIV. | | | 32,600 | | |
| XV. | | 40,600 | | | |
| XVI. | | | 12,080 | | |
| XVII. | | | 40,400 | | |
| XVIII. | | | (?) | | |
| XIX. | | 35,600 | | | |
| XX. | | 44,000 | | | |
| XXI. | | | | 13,000 | |
| XXII. | | | 16,300 | | |
| XXIII. | | | | 25,000 | |

Table No. XXIII shows it to be just as true that no relation to age, severity of the disease, or prognosis can be demonstrated in these cases.

TABLE NO. XXIII.—RELATION OF LEUCOCYTOSIS TO AGE, SEVERITY OF DISEASE, AND PROGNOSIS

| Case No. | Acute. Mild. | Severe. | Very severe. | Fulminating. | Chronic. | Result. | Age. |
|---|---|---|---|---|---|---|---|
| V. | | | 40,800 | | | | Between 1 and 2 yrs. |
| IV. | | | 45,000 | | | | Between 2 and 5 yrs |
| XVII. | | | 40,400 | | | | |
| II. | | | | | 30,000 | | Between 5 and 10 yrs. |
| VIII. | | 23,400 | | | | | |
| IX. | | | 30,000 | | | | |
| X | 26,800 | | | | | | |
| XI. | | 16,400 | | | | | |
| XII. | | 43,400 | | | | | |
| XIV. | | | 32,600 | | | | |
| XIX. | | 35,600 | | | | | |
| III. | | | 24,000 | | | | Between 10 and 20 yrs. |
| XV. | | 40,600 | | | | | |
| XX. | | 44,000 | | | | | |
| XXIII. | 25,000 | | | | | | |
| I. | | | | | (?) | | Over 20 years. |
| VI. | | 24,000 | | | | | |
| VII. | | | | 24,000 | | | |
| XIII. | | | 36,080 | | | | |
| XVI. | | 12,080 | | | | | |
| XVIII. | (?) | | | | | | |
| XXI. | | | 13,000 | | | | |
| XXII. | 16,300 | | | | | | |

Of course the degree of leucocytosis depends upon both the severity of the infection and the resistance of the individual. Distinctions may be drawn, however, between leucocytosis above and below 20,000. A leucocyte count above 20,000 is a well-marked outspoken reaction. Of the 4 cases with counts below 20,000, Cases Nos. XI and XXII were mild or moderately severe infections. Cases No. XVI and XXI were men with very poor resistance, one of them suffering a relapse and the other dying ultimately.

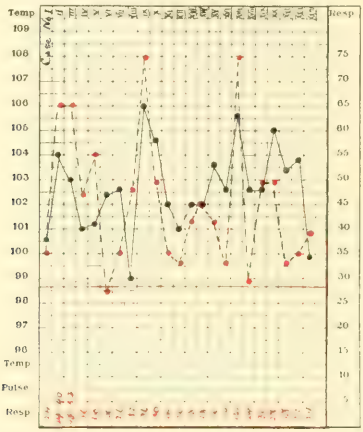
In Case No. VIII small diplococcus-like bodies were seen within the leucocytes in the circulating blood, in fresh blood and stained specimens. They were Gram negative. But they failed to grow in a blood culture.

7. Pulse, Temperature, and Respirations.—A study of the cases in regard to the temperature upon admission, before serum, shows nothing distinctive or remarkable. The character of the temperature between onset and admission was noted in only a few cases.

Case No. I, chronic in type, after an acute febrile course of 12 days, suffered several paroxysms of fever and intensification of symptoms, and was apparently afebrile in the intervals.

Case No. II, also chronic, had run an intermittent type of fever for 4 weeks, the temperature reaching 105° F. each afternoon.

In no other cases were actual observations made, the note being as a rule, "high fever persisting."




A Composite Chart of the Temperature, Pulse, and Respirations of the 23 Cases on Admission Before the Administration of Serum.
Solid line = temperature. Broken line = pulse.

The above chart shows that only 3 of the cases had a temperature below 101° F., before serum, and 3, 105° F. or above

The pulse, before the first puncture, one would expect to be slow and the intracranial pressure high. The 8 cases with pulse 100 or below to the minute, immediately before the punctures, had intraspinal pressures as follows:

| Case No. | Mm. | Pulse. |
|---|---|---|
| VI | 170 | 84 |
| VII | 210 | 100 |
| XI | 210 | 100 |
| XII | 380 | 96 |
| XVI | 200 | 96 |
| XVIII | 330 | 88 |
| XXI | 160 | 96 |
| XXII | 380 | 100 |

Considering the normal as 80-120 mm., these show only a moderately low grade of increased pressure (see Table No. VI). On the other hand the 5 cases with pulse 140 or plus, showed a higher grade of increased pressure:

| Case No. | Mm. | Pulse. |
|---|---|---|
| II | 400 | 160 |
| III | 400 | 160 |
| V | 400 | 140 |
| IX | 410 | 180 |
| XVII | 300 | 180 |

Looking at the question from another point of view, the cases may be divided as follows:

First, those with a moderately low grade of increased pressure (below 350 mm.) as follows:

| Case No. | Mm. | Pulse. |
|---|---|---|
| IV | 180 | 124 |
| VI | 170 | 84 |
| VII | 210 | 100 |
| X | 200 | 128 |
| XI | 210 | 100 |
| XVI | 200 | 96 |
| XVII | 300 | 180 |
| XVIII | 330 | 88 |
| XIX | 180 | 129 |
| XX | 260 | 129 |
| XXI | 160 | 96 |

These are 11 of 22 cases. The lowest pulse is 84, the highest 180, and the average 114.

Second, those with a high grade of increased pressure (350 mm. and plus):

| Case No. | Mm. | Pulse. |
|---|---|---|
| II | 400 | 160 |
| III | 400 | 160 |
| V | 400 | 140 |
| VIII | 400 | 126 |
| IX | 410 | 180 |
| XII | 380 | 96 |
| XIII | 600 | 112 |
| XIV | 550 | 120 |
| XV | 500 | 112 |
| XXII | 380 | 100 |
| XXIII | 400 | 108 |

This class also consists of 11 cases. The lowest pulse is 96, the highest 180, and the average 138.

In *summary* then, the cases with the higher grades of increased pressure show the more rapid pulse (average 138), and those with lower grades of increased pressure have the slower pulse (average 114).

In this consideration the age of the patients and the degree of intoxication and exhaustion should be factors. The respirations show nothing of interest. The highest temperature is accompanied by the more rapid respiratory rate. Irregular breathing, or the Cheyne-Stokes' type, proved a bad omen in Case No. IV. He died of a respiratory paralysis.

8. Confirmation of Clinical Diagnosis.—On admission to the ward, as soon as possible after a history had been taken and a physical examination and leucocyte count made, the first lumbar puncture was performed. This procedure aimed to confirm the clinical diagnosis of meningitis and determine the type by 4 manifestations, to wit:

(1) Pressure of the fluid in the subarachnoid space.

(2) Macroscopic examination of the spinal fluid.

(3) Microscopic examination of the spinal fluid.

(4) Cultivation of *Diplococcus intracellularis meningitidis.*

(1) *Pressure of the Spinal Fluid.*—The spinal fluid was under increased pressure in the subarachnoid space in every case. The pressures recorded at the first puncture are tabulated and discussed in detail above (Section II, 3 and 4). The average pressure at the first puncture was 327 mm., the highest 600+ mm., and the lowest 160 mm.

(2) *Macroscopic Examination of the Spinal Fluid.*—Cloudiness of the fluid at the first tap has been the indication for giving serum in some clinics. Nineteen of the 23 specimens of fluid at first puncture in this series showed varying degrees of cloudiness (as shown by Table No. XXIV).

TABLE No. XXIV.—CHARACTER OF SPINAL FLUID MACROSCOPICALLY.

| Faintly cloudy. | Cloudy. | Very cloudy. | Very densely cloudy. | Purulent. | Clear with flocculi. |
|---|---|---|---|---|---|
| | I. | | | | II. |
| | | III. | | | IV. |
| | V. | | | | |
| | | VI. | | | |
| | | | VII. | | |
| | VIII. | | | | |
| | | | IX. | | |
| X. | | | | | |
| XI. | | | | | |
| | | XII. | | | |
| | | XIII. | | | |
| | | XIV. | | | |
| | | XV. | | | |
| | | XVI. | | | |
| | | | | | XVII. |
| | | XVIII. | | | |
| | XIX. | | | | |
| XX. | | | | | |
| | | XXI. | | | |
| | | | | XXII. | |
| | | | | | XXIII. |
| 3 | 4 | 9 | 2 | 1 | 4 |

However, 4 cases had a clear, limpid fluid which contained fine flocculi in smaller or greater amounts.

TABLE No. XXV.—THE FOUR CASES WITH CLEAR SPINAL FLUID AT FIRST PUNCTURE.

| Case. | Day of 1st puncture. | Pressure. | Cell content. | Bacteria in smears. | By culture. |
|---|---|---|---|---|---|
| II. | 44 | 100 | P.m.n.* 38% S.m.n. * 62% | A few extracellular diplococci. | Very scanty growth. |
| IV. | 14 | 180 | A few cells: s. m.n. predominating. | Do. | 4 colonies per tube. |
| XVII. | 7 | 300 | Débris. | Do. | 1 colony per tube. |
| XXIII. | 6 | 400 | A few cells: p. m.n. predominating. | None. | No growth. |

* P.m.n. = polymorphonuclear; S.m.n. = small mononuclear.

All 4 showed an increase in the intraspinal pressure. In Cases Nos. II and IV the fluid resembled a tuberculous spinal fluid in cell content, small mononuclear leucocytes predominating. But a few extracellular diplococci were seen in smears, and cultures gave a scanty growth. Case No. XXIII had polymorphonuclears predominating, the flocculi in all these 3 cases being clumps of cells. Case No. XVII showed diplococci and cellular débris, the culture being positive. In Case No. XXIII no organisms were recovered by smear or culture at the first tapping, but they were found in specimens from the second tapping, no serum having been given in the interval.

The tuberculous-like spinal fluids were seen in subacute or chronic cases, as would be expected. It is well to bear in mind that the clearness of the spinal fluid is no indication of its sterility.

(3) *Microscopic Examination of the Spinal Fluid* consisted in the study of smears of the centrifugalized sediment for the identification of cells and organisms. The 4 cases with clear fluid have been considered above. The 19 with cloudy fluid showed cells varying in number according to the cloudiness. In all 19 the predominating cell was the polymorphonuclear leucocyte. In 8 of them small mononuclear leucocytes and large endothelial cells were noted.

In all but 2 of the 23 cases, Gram-negative diplococci were found. In these 2 they were recovered by culture. The distribution of these organisms was as follows:

| | Cases. |
|---|---|
| Equally intracellular and extracellular | 8 |
| Both intracellular and extracellular but mainly extracellular | 6 |
| Same, but mainly intracellular | 1 |
| Entirely extracellular | 4 |
| Entirely intracellular | 2 |

(4) *Cultivation of the Diplococcus intracellularis meningitidis* from the centrifugalized sediment, upon glycerine agar, was accomplished in 22 of 23 cases. In Case No. VI they were positively identified by morphological and tinctorial characteristics in smears of the sediment, but were not viable.

In *summary,* then, the clinical diagnosis was confirmed in every case by the cytological and bacteriological examination of the spinal fluid.

## V. The Effect of the Serum.

As a new therapeutic measure, it was fitting that the effect of the serum should be studied most carefully, both at the bedside and in the laboratory. The general results are exhibited above. The following pages contain in detail the steps to that end.

### AT THE BEDSIDE.

1. The Temperature Chart.—(a) *The Temperature.*—This, with the pulse and respirations, was observed every 2 hours. The records were taken per rectum. The Composite Chart (Section IV) shows the temperature, pulse, and respirations of the cases upon admission to the wards, which practically means immediately before serum. The temperature charts attached to the protocols (Section VI) show the records before and after serum in the individual cases. The following tables are an effort to bring these records together in concise form for consideration.

TABLE No. XXVI.—INFLUENCE OF FIRST INJECTION UPON TEMPERATURE.

| Case No. | Character. | Highest previous Temp. | First Injection of Serum. Temperature.* | | | Course. |
|---|---|---|---|---|---|---|
| | | | Before. | Immediate effect. | Later effect. | |
| I. | Chronic. | 100.6° F. | 99.7° F. | ? (Temp. q. 4 h.) | 98.0° F. in 10 hrs. | Second injection. |
| II. | Subacute. | 101.8° | 100.0° | 102.4° F. in 4 hrs. | 98.6° " 20 " | " " |
| III. | Acute. | 103.2° | 103.2° | 103.8° " 6 " | 100.4° " 26 " | " " |
| IV. | In collapse. | 101.0° | 98.5° | { 98.5° for 8 " / 103.0° in 16 " } | 100.8° " 20 " | " " |
| V. | In collapse. | 101.4° | 97.0° | 102.0° " 8 " | 97.4° " 16 " | " " |
| VI. | Acute. | 102.4° | 102.4° | 102.6° " 4 " | 99.6° " 22 " | " " |
| VII. | Fulminant. | 102.6° | 103.8° | 105.4° " 12 " | 105.4° " 12 " | " " |
| VIII. | Acute. | 99.0° | 99.0° | 99.7° " 4 " | 99.0° " 12 " | " " |
| IX. | Acute. | 106.0° | 106.0° | 98.0° " 10 " | 102.0° " 14 " | " " |
| X. | Acute. | 104.6° | 102.3° | Constant fall to | 99.2° " 28 " | Remained below 100° F. |
| XI. | Acute. | 102.0° | 100.2° | { 99.8° in 8 " / 102.4° " 12 " } | 99.7° " 40 " | Second injection. |
| XII. | Acute. | 101.0° | 101.0° | 98.8° " 10 " | 101.1° " 22 " | " " |
| XIII. | Acute, complicated. | 101.6° | 101.6° | 102.0° " 2 " | 101.6° " 14 " | " " |
| XIV. | Acute, complicated. | 102.0° | 102.0° | 102.0° for 6 " | 101.0° " 10 " | " " |
| XV. | Acute. | 103.6° | 103.6° | 98.6° in 12 " | 100.8° " 16 " | " " |
| XVI. | Acute. | 102.6° | 100.0° | 101.6° " 4 " | 98.4° " 24 " | " " |
| XVII. | Acute, complicated. | 105.6° | 105.5° | 101.4° " 18 " | Rose to 103° with acute lobar pneumonia. | |
| XVIII. | Acute. | 103.0° | 100.4° | 101.4° " 8 " | 100.6° in 12 hrs. | Second injection. |
| XIX. | Acute. | 102.6° | 102.6° | 106.4° " 10 " | 104.8° " 14 " | " " |
| XX. | Acute. | 104.2° | 102.6° | 105.3° " 8 " | 103.2° " 16 " | " " |
| XXI. | Acute. | 104.0° | 101.5° | 99.9° " 6 " | 103.0° " 14 " | " " |
| XXII. | Acute. | 104.0° | 103.5° | 103.9° " 4 " | 98.5° " 16 " | Slight rise each day for 1 week. |
| XXIII. | Acute. | 99.8° | 99.6° | 99.2° " 4 " | { 102.5° " 8 " / 100.0° " 20 " } | Irregular fever for 2 weeks. |

* All temperatures recorded in this and other charts are Fahrenheit.

TABLE No. XXVII. INFLUENCE OF SECOND AND THIRD INJECTIONS UPON TEMPERATURE

| Case No. | Second Injection of Serum — Temperature. Before. | Immediately after. | Later. | Third Injection of Serum. Temperature. Before. | Immediately after. | Later. | Course. |
|---|---|---|---|---|---|---|---|
| I. | 98.7° F. | ? (Temp. q. 4 h.) | 98.2° F. in 8 hrs. | Remained below 99° F. after second injection. | | | |
| II. | 98.6° | 101.3° F. in 16 hrs. | 98.0° " 44 " | 98.4° F. | 99.0° F. in 24 hrs. | 98.6° F. in 32 hrs. | Slight rise each day for 2 weeks. |
| III. | 100.4° | 102.6° " 2 " | 101.2° " 20 " | 101.6° | 102.4° " 2 " | 99.0° " 56 " | Fourth, fifth and sixth injections. |
| IV. | 102.8° | 101.6° " 8 "<br>104.4° " 16 " | 98.5° " 20 " | Paralysis of respiration and death. | | | |
| V. | 96.4° | 96.0° " 4 "<br>98.2° " 20 " | 98.0° " 21 " | 98.0° | 100.4° in 8 hrs. | 98.0° " 20 " | Remained normal; fourth injection. |
| VI. | 99.6° | 101.3° " 18 " | 98.6° " 26 " | Slight rise each day for 2 weeks. | | | |
| VII. | 105.2° | 103.1° " 4 " | 102.7° " 8 " | 102.7° | 103.1° in 4 hrs. | 101.8° " 16 " | Fourth and fifth injections; death. |
| VIII. | 99.1° | 101.2° " 8 " | 100.4° " 16 " | 100.4° | 100.0° " 4 "<br>103.0° " 8 " | 100.3° " 16 " | Fall to normal in 1 week. |
| IX. | 102.0° | 103.7° " 8 " | 102.4° " 18 " | 103.8° | 100.1° " 14 " | 103.0° " 48 " | Fourth, fifth and sixth injections. |
| X. | Normal after one injection. | | | | | | |
| XI. | 100.0° | 98.6° in 4 hrs.<br>100.6° " 12 " | 98.6° " 28 " | Remained normal. | | | |
| XII. | 100.2° | 98.8° " 2 " | Slight rise each day for 1 week—relieved by paracentesis tympani. | | | | |
| XIII. | 102.4° | 102.8° " 2 " | 102.2° in 10 hrs. | 102.2° | 103.0° in 2 hrs. | Death in 10 hrs. | |
| XIV. | 101.8° | 102.3° " 4 " | 100.6° " 18 " | Bronchopneumonia—third and fourth injections had no influence. | | | |
| XV. | 100.8° | 101.6° " 2 " | 99.3° " 14 " | Slight rise each day for 5 days. | | | |
| XVI. | 98.4° | 101.2° " 4 " | 100.0° " 16 " | 100.8° | 101.7° in 4 hrs. | 99.6° in 12 hrs. | Intermittent fever 10 days; fourth injection. |
| XVII. | Pneumonia—uninfluenced by second injection—lysis—otitis media—empyema—operation. | | | | | | |
| XVIII. | 101.1° | 98.4° in 6 hrs. | Remained normal except for slight rise next day. | | | | |
| XIX. | 101.8° | 98.7° " 10 " | 105.4° in 26 hrs. | 105.4° | 98.8° in 6 hrs. | 103.4° in 36 hrs. | Rapid fall to normal. |
| XX. | 101.0° | 98.0° " 24 " | Remained normal. | | | | |
| XXI. | 102.0° | 100.0° " 7 " | 101.6° in 22 hrs. | 99.8° | 101.8° in 6 hrs. | 99.8° in 18 hrs. | Irregular fever for 43 days; 17 punctures; 12 injections; no influence. |
| XXII. | Needed but one injection. | | | | | | |
| XXIII. | " " " " | | | | | | |

Seven cases received a fourth injection of serum:

TABLE NO. XXVIII.—INFLUENCE OF FOURTH INJECTION UPON TEMPERATURE.

| Case No. | Fourth Injection of Serum. Temperature. Before. | Immediately after. | Later. | Course. |
|---|---|---|---|---|
| III. | 102.8° F. | 103.2° F. in 4 hrs. | 99.7° F. in 38 hrs. | Fifth and sixth injections. |
| V. | 98.7° | 102.6° " 8 " | 98.5° " 20 " | Remained normal. |
| VII. | 101.8° | 102.0° " 4 " | 102.4° " 8 " | Fifth injection. |
| IX. | 103.0° | 104.6° " 60 " | 100.3° " 18 " | Fifth and sixth injections. |
| XIV. | 102.8° | 103.4° " 4 " | 101.8° " 16 " | Pneumonia; below 100° in 2 weeks; third and fourth injections; no influence. |
| XVI. | 102.6° | 98.4° " 24 " | Remained normal. | |
| XXI. | 101.3° | 101.6° " 8 " | 99.2° in 14 hrs. | Irregular fever 43 days; injections without influence. |

Four cases received further injections. Case No. XXI received in all 12 injections of serum, but after the first 4 the spinal fluid became sterile and the temperature was not influenced apparently.

TABLE NO. XXIX.—INFLUENCE OF FIFTH AND SIXTH INJECTIONS UPON TEMPERATURE.

| Case No. | Fifth Injection of Serum. Temperature. Before. | Immediately after. | Later. | Course. |
|---|---|---|---|---|
| III. | 103.8° F. | 104.6° F. in 8 hrs. | 98.6° F. in 52 hrs. | Sixth injection. |
| VII. | 102.4° | 104.2° " 24 " | and death. | |
| IX. | 104.2° | 104.5° " 5 " | 99.3° in 13 hrs. | Sixth injection. |
| | Sixth Injection. | | | |
| III. | 102.8° | 103.3° in 6 hrs. | 98.6° in 20 hrs. | Normal after 3 days. |
| IX. | 105.2° | 98.2° " 35 " | Remained normal. | |

Temperature Reaction, Temporary Effect: A glance at these tables shows that the temperature has behaved, in general, in four different ways after injections of serum, to wit:

(1) Preliminary rise and subsequent fall, 36 instances.

(2) Fall alone, 10 instances.

(3) Preliminary fall and subsequent rise, 8 instances.

(4) No effect, 12 instances.

This is in a total of 66 instances recorded above. The relative frequency of the various reactions is approximately the same, whether it be after the first, second, or third injection.

TABLE No. XXX.—CHARACTER OF TEMPERATURE REACTION AFTER SUCCESSIVE INJECTIONS.

| Character of reaction. | After injection number | | | | | | |
|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | |
| 1. Rise and fall | 9 | 9 | 7 | 4 | 1 | 0 | Instances. |
| 2. Fall | 6 | 5 | 0 | 1 | 1 | 2 | " |
| 3. Fall and rise | 4 | 2 | 2 | 0 | 0 | 0 | " |
| 4. No effect | 3 | 3 | 2 | 2 | 2 | 1 | " |

(1) The preliminary rise of temperature and subsequent fall was the most common form of reaction, occurring in 55 per cent of the instances. This, as will be shown later, was accompanied by an increased, temporary restlessness and discomfort. It can be explained by the bactericidal action of the serum, and should occur in the more flourishing infections, where a greater number of organisms are destroyed and their toxins liberated. These are the cases in which we advise combining subcutaneous with intraspinal employment of the serum. The character of the infection in these cases will be considered later under the bacteriological studies.

(a) In 5 of these 36 instances the rise was preceded by a period of 2 to 8 hours, in which the temperature remained practically the same:

TABLE No. XXXI.—TEMPERATURE REACTION AFTER SERUM.—LATE RISE AND FALL, AFTER INTERVAL OF QUIESCENCE.

| Case No. | 1st injection: Before. | After. | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| IV. | 98.5° F.; | 98.5° F. | for 8 hrs.; | 103.0° F. | in 16 hrs.; | 100.8° F. | in 20 hrs. | | |
| XI. | 100.2° | 98.8° | " 8 " | 102.4 | " 12 " | 99.7 | " 40 " | | |
| XXIII. | 99.6° | 99.2° | " 2 " | 102.5° | " 8 " | 100.0° | " 20 " | | |
| | 2d injection: | | | | | | | | |
| IV. | 102.8° | 101.6° | " 8 " | 104.4 | " 16 " | 98.5 | " 20 " | | |
| | 3d injection: | | | | | | | | |
| VIII. | 100.4° | 101.0° | " 4 " | 103.0 | " 8 " | 100.3 | " 16 " | | |

The quiescent period was 6 hours on the average. A rise of 2.8° to 4.5° F., average 3.4° F., occurred in 8 to 16 hours after the injection. The low point, the late effect of the injection, was reached in 16 to 40 hours, an average of 23 hours.

(b) The majority of reactions, however, resulted in an immediate, preliminary rise and subsequent fall.

TABLE No. XXXII.—TEMPERATURE REACTION AFTER SERUM, RISE AND FALL.

| Case No. | Temp. before. | Rise. | | Fall. | |
|---|---|---|---|---|---|
| **1st injection:** | | | | | |
| II. | 100.0° F. | 102.4° F. | in 4 hrs. | 98.6° F. | in 20 hrs. |
| III. | 103.2° | 103.8° | " 6 " | 100.4° | " 26 " |
| V. | 97.0° | 102.0° | " 8 " | 97.4° | " 16 " |
| VI. | 102.4° | 102.6° | " 4 " | 99.6° | " 22 " |
| VIII. | 99.0° | 99.7° | " 4 " | 99.0° | " 12 " |
| XVI. | 100.0° | 101.6° | " 4 " | 98.4° | " 24 " |
| XVIII. | 100.4° | 101.4° | " 8 " | 100.6° | " 12 " |
| XIX. | 102.6° | 106.4° | "10 " | 104.8° | " 14 " |
| XX. | 102.6° | 105.3° | " 8 " | 103.2° | " 16 " |
| XXII. | 103.5° | 103.9° | " 4 " | 98.5° | " 16 " |
| **2d injection:** | | | | | |
| II. | 98.6° | 101.3° | "16 " | 98.0° | " 44 " |
| III. | 100.4° | 102.6° | " 2 " | 101.2° | " 20 " |
| VI. | 99.6° | 101.3° | "18 " | 98.6° | " 26 " |
| VIII. | 99.1° | 101.2° | " 8 " | 100.4° | " 16 " |
| IX. | 102.0° | 103.7° | " 8 " | 102.4° | " 18 " |
| XIV. | 101.8° | 102.3° | " 4 " | 100.6° | " 18 " |
| XV. | 100.8° | 101.6° | " 2 " | 99.3° | " 14 " |
| XVI. | 98.4° | 101.2° | " 4 " | 100.0° | " 16 " |
| **3d injection:** | | | | | |
| II. | 98.4° | 99.0° | "24 " | 98.6° | " 32 " |
| III. | 101.6° | 102.4° | " 2 " | 99.0° | " 56 " |
| V. | 98.0° | 100.4° | " 8 " | 98.0° | " 20 " |
| VII. | 102.7° | 103.4° | " 4 " | 101.8° | " 16 " |
| XVI. | 100.8° | 101.7° | " 4 " | 99.6° | " 12 " |
| XXI. | 99.8° | 101.8° | " 6 " | 99.8° | " 18 " |
| **4th injection:** | | | | | |
| III. | 102.8° | 103.8° | " 4 " | 99.7° | " 38 " |
| V. | 98.7° | 102.6° | " 8 " | 98.5° | " 20 " |
| IX. | 103.0° | 104.6° | " 6 " | 100.3° | " 18 " |
| XXI. | 101.3° | 101.6° | " 8 " | 99.2° | " 14 " |
| **5th injection:** | | | | | |
| III. | 103.2° | 104.6° | " 8 " | 98.6° | " 52 " |
| IX. | 104.2° | 104.5° | " 5 " | 99.3° | " 13 " |
| **6th injection:** | | | | | |
| III. | 102.8° | 103.3° | " 6 " | 98.6° | " 20 " |

The 31 instances of this type show a rise from 0.2° to 5.0° F. in 2 to 24 hours, averages of 1.7° rise in 7 hours. The low point was reached in 12 to 56 hours, average of 22 hours. This end-effect was obtained in approximately the same time as in the type with preceding quiescent period.

(2) An immediate fall occurred in 15 per cent of the instances. In 3 of these (b), the next injection was given before the temperature had fallen below 101° F.

It is probable that it would not have continued to fall to normal inasmuch as two of the cases were developing complicating pneumonia, and the third case was fulminant and eventually fatal.

TABLE No. XXXIII.—TEMPERATURE REACTION AFTER SERUM—FALL.

(*a*).

| Case No. | 1st injection: Temp. before. | Result. | |
|---|---|---|---|
| X. | 102.3° F. | 99.2° F. | in 28 hrs. |
| | 2d injection: | | |
| XI. | 100.0° | 98.6° | " 28 " |
| XII. | 100.2° | 98.8° | " 2 " |
| XVIII. | 101.1° | 98.4° | " 6 " |
| XX. | 104.0° | 98.0° | " 24 " |
| | 4th injection: | | |
| XVI. | 102.6° | 98.4° | " 24 " |
| | 6th injection: | | |
| IX. | 105.2° | 98.2° | " 35 " |

(*b*).

| | 1st injection: | | |
|---|---|---|---|
| XIV. | 102.0° | 101.0° | " 10 " |
| XVII. | 105.5° | 101.4° | " 18 " |
| | 2d injection: | | |
| VII. | 105.2° | 102.7° | " 8 " |

The constant fall to normal (a) occurred in the other 7 cases. It is striking that in each instance of this type of reaction the temperature remained normal and the attack was terminated successfully thereby. Such a fall is a good omen, therefore, but one may be misled in prediction by the third type where the fall is preliminary to a rise. This fall of 1.4° to 7.0° F., average 3.7°, has occupied from 2 to 28 hours, an average of 21 hours.

(3) The preliminary fall and subsequent rise occurred in 12 per cent of the instances:

TABLE No. XXXIV.—TEMPERATURE REACTION AFTER SERUM FALL AND RISE.

| Case No. | Temp. before. | Fall. | Rise. |
|---|---|---|---|
| 1st injection: | | | |
| IX. | 106.0° F. | 98.0° F. in 10 hrs. | 102.0° F. in 14 hrs. |
| XII. | 101.0° | 98.8° " 10 " | 101.1° " 22 " |
| XV. | 103.6° | 98.6° " 12 " | 100.8° " 16 " |
| XXI. | 101.5° | 99.9° " 6 " | 103.0° " 14 " |
| 2d injection: | | | |
| XIX. | 104.8° | 98.7° " 10 " | 105.4° " 26 " |
| XXI. | 102.0° | 100.0° " 7 " | 101.6° " 22 " |
| 3d injection: | | | |
| IX. | 103.8° | 100.1° " 14 " | 103.0° " 48 " |
| XIX. | 105.4° | 98.8° " 6 " | 103.4° " 36 " |

In every instance but one, a succeeding injection was given during the period of secondary rise. In this one, Case No. XIX, third injection, a second fall in 44 hours brought the temperature to a normal level, where it remained. The preliminary fall to normal occupied 6 to 14 hours, an average of 9 hours. The propitious type (Table XXXIII) required 21 hours to reach normal, almost as long as this type (Table XXXIV) takes to reach the acme of the secondary rise (14 to 48 hours, an average of 25 hours). The more rapid fall then is more apt not to be permanent.

(4) Practically no effect upon the temperature was recorded in 12 instances (18 per cent). Three of these were after the first, fourth, and fifth injections in Case No. VII, the fulminant case, in which the serum was given every 12 hours. The temperature was constantly elevated.

Case No. V, in collapse, had a temperature of 96.4° F. before the second injection of serum. This returned to normal as he improved. Cases Nos. XIII, XIV, and XVII were complicated by pneumonia, which masked any possible temperature reaction. Case No. XXI was complicated by hydrocephalus. These 4 cases include 8 instances.

Temperature Reaction—Permanent Effect: In most cases, the serum was given repeatedly day by day, or even more often, until the temperature remained normal and the symptoms and other signs suggested that the process was clearing. Subtracting 4 fatal cases (Nos. IV, VII, XIII, and XXI) and 2 cases complicated by pneumonia (Nos. XIV and XVII), there remain 17 cases which cleared up as a direct consequence of the injections of serum.

TABLE NO. XXXV.—TEMPERATURE REACTION OF LAST INJECTION IN CASE OF RECOVERY.

| Injection No.: | 1 | 2 | 3 | 4 | 5 | 6 | Total. |
|---|---|---|---|---|---|---|---|
| 1. Rise and Fall: | XXII. XXIII. | VI. XV. | II. (V).. ....V. VIII. | | | III. | 8 |
| 2. Fall: | X. | I. (?) XVIII. XI. XX. XII. | | XVI. | | IX. | 8 |
| 3. Fall and Rise: | | | XIX. | | | | 1 |
| Total: | 3 | 7 | 3 | 2 | 0 | 2 | 17 |

The reactions in these instances are equally divided between a temporary rise and subsequent fall and an immediate fall. The largest number of cases (7) cleared up after the second injection, as compared to 3 after the first and 3 after the third injections. But it is noteworthy that in 6 of these 7 cases, the spinal fluid was rendered sterile by the first injection. It is possible that the one injection would have proved sufficient. Cases Nos. III and IX were persistent infections, each requiring 6 injections, in spite of the fact that the first 3 were given at 24-hour intervals. Case No. V really resolved after the third injection. The fourth was given some time after the temperature was normal on account of the apparent blindness.

Those cases in which the temperature fell to normal in about 24 hours after the injection of serum have been classified as "abrupt recoveries."

TABLE NO. XXXVI.—ABRUPT RECOVERY—9 CASES.

| Case No. | Temperature. | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| I. | Normal | 8 hrs. | after | 2d | injection: | 38 hrs. | after | 1st | injection. | |
| X | " | 14 | " | " | 1st | " | | | | |
| XI. | " | 14 | " | " | 2d | " | 36 | " | " | " |
| XII. | " | 16 | " | " | 2d | " | 36 | " | " | " |
| XVI. | " | 24 | " | " | 4th | " | 13 dys. | " | " | " |
| XVIII. | " | 4 | " | " | 2d | " | 24 hrs. | " | " | " |
| XIX. | " | 6 | " | " | 3d | " | 54 | " | " | " |
| XX. | " | 26 | " | " | 2d | " | 52 | " | " | " |
| XXII. | " | 12 | " | " | 1st | " | | | | |

Nine cases resolved in this manner:

2 required a single injection.
5 required 2 injections.
1 required 3 injections.
1 required 4 injections.

This resolution took from 4 to 26 (average 14) hours after the last injection, and from 24 hours to 13 days after the first injection. The latter figures are not so important, inasmuch as they depend upon the frequency of the injections.

Two cases terminated by a "less abrupt recovery," requiring, the one, 36 hours, and the other, 60 hours, but the temperature falling constantly during this time:

TABLE NO. XXXVII.—LESS ABRUPT RECOVERY—2 CASES.

| Case No. | Temperature. |
|---|---|
| III. | Normal 60 hrs. after 6th injection; 16 dys. after 1st injection. |
| IX. | " 36 " " 6th " 8 " " " " |

It is interesting that these two cases are the most persistent ones of the series, both needing 6 injections before resolution.

Any time longer than this has been termed "lysis." Six cases have recovered in this manner:

TABLE NO. XXXVIII.—RECOVERY BY LYSIS—6 CASES.

| Case No. | Temperature. |
|---|---|
| II. | Normal 2 wks. after 3d injection; 17 dys. after 1st injection. |
| V. | " 4 dys. " 3d " 6 " " " " |
| VI. | " 11½ " " 2d " 12½ " " " " |
| VIII. | " 7 " " 3d " 9 " " " " |
| XV. | " 6 " " 2d " 7 " " " " |
| XXIII. | " 15 " " 1st " |

They have required from 4 to 15 days to reach a permanent normal level. In 3 cases lysis occurred after the third injection, 2 after the second, and 1 after the first. This accounts for 17 cases. In addition 2 were complicated by pneumonia, and 4 died.

To *summarize*: Classifying the cases of "less abrupt recovery" with "lysis," "abrupt recovery" occurred in 53 per cent and "lysis" in 47 per cent of the series.

We prefer to reserve the term "relapse" for those cases in which the specific micro-organisms reappear in a spinal fluid already rendered sterile by serum, instead of applying it to a flare-up of temperature alone. In this sense there were two instances of relapse in the series, Cases Nos. XVI and XXI.

Finally, attention must be called to the type of temperature exhibited by Case No. XVI. A febrile paroxysm occurred daily, preceded by a chill, and accompanied by headache and dullness. In the intervals he enjoyed comfort. It is well to keep in mind that such a chart (Section VI, No. XVI) may be caused by a simple meningitis without complications.

(b) *The Pulse.*—Before the use of serum it is described in Section IV. There it was pointed out that the more rapid pulse was associated with the higher grades of increased intracranial pressure and the slower pulse with the lower grades.

The same conditions appeared to exist after the use of serum. The pulse was of no use as an indicator for puncturing. One might expect the pulse to become less rapid as the intracranial pressure was raised by the reaccumulation of exudate, but in no single instance did this occur. Nor did the injection of serum, in even larger amounts than fluid removed, result in a slow pulse. In the majority of instances the pulse rose and fell in normal ratio with the temperature. So, as a rule, when it was considered that a puncture and injection were indicated, namely, when the temperature rose or continued elevated, the pulse was usually found correspondingly increased. Koplik * would not do a lumbar puncture unless there are signs of increased intracranial pressure, particularly the so-called MacEwen's sign of hydrocephalus. But it is our experience that continuation of the temperature or a subsequent rise without complications indicates that a spinal fluid still containing virulent diplococci will be found upon puncture to be sufficient justification for the procedure. In Cases Nos. I, II, III, VIII, IX, X, XII, XV, XIX, XX, XXII, and XXIII, 12 cases, the pulse followed the temperature in its rise and fall. In 3 mild cases (Nos. VI, XVI, and XVIII) a bradycardia was present throughout. The fatal cases (Nos. IV, VII, XIII, XXI) had more and more marked tachycardia as death approached. Seven cases (Nos. III, V, VIII, IX, XI, XIV, XVII) had a tachycardia at one time or another. Of these, Cases Nos. III and IX were severe intoxications, but in both the pulse fell with the improvement after the use of serum. No. V was a baby well worn out by the attack. Cases Nos. XIV and XVII were complicated by pneumonia, and Case No. VIII had a definite myocarditis.

(c) *Respirations.*—Just as with the pulse, the effect of the serum upon the respirations amounted to an improvement hand-in-hand with

* Loc. cit.

the general relief. In the fatal cases they varied between 44 and 60 per minute. Cases Nos. IV and XXI died by respiratory paralysis, apparently the common mode of death in these cases. The pneumonia cases, of course, had rapid respirations, 28 to 80—Cases Nos. XIII, XIV, and XVII. The irregular respirations, Cheyne-Stokes' type, and occasional cessations in No. XXI, were uninfluenced by serum injections. But in the other 17 cases the respirations were increased or slowed with the rises and falls of temperature, and returned to normal with the improvement after the use of serum.

2. Symptoms.—Much more striking than any other feature is the effect of the serum upon the symptoms. The most prominent symptoms have been:

(1) The headache, hyperæsthesia, and various pains in the limbs and over the body; and

(2) The mental condition, delirium, stupor, unconsciousness, and convulsions.

These more or less hand-in-hand with the course of the temperature have been influenced in two ways:

(a) A temporary intensification with the preliminary rise of temperature.

(b) A permanent relief with the subsequent fall of temperature.

(1) *Temporary Intensification.*—In 31 instances the injection of serum was followed first by a rise in temperature lasting 7 hours on the average, and then by a fall. During the short period of rise of temperature certain symptoms were intensified. The patients were more restless and irritable; the headache was increased. Some were severely intoxicated, stupid, or irrational; others complained of backache and pains about the body.

(2) *Permanent Relief.*—This was followed, however, sooner or later, by a remarkable relief. As a rule, sinking into a deeper, more natural sleep than previously, they would awake to be brighter, more cheerful, and actively interested in their surroundings.

For instances we will quote from the histories:

Case No. II, after the first injection of serum: "The temperature reached normal in 14 hours. More marked was the change in the general condition. After a good sleep the child awoke, bright and cheerful. He noticed his surroundings for the first time and chatted about home. However, for a few hours immediately following the puncture, he cried and complained of headache."

Case No. III, after the second injection: "During the next 24 hours the improvement was great. He became rational and recognized his family."

Case No. VIII, after the second injection: "Twelve hours later his headache had disappeared and his mind was clear. But the retracted head, stiff neck, and arched back persisted."

Case No. IX, after the sixth injection: "The improvement in the next 48 hours was marked. The temperature fell steadily from 104.8° to 99.8° F. From stupor he became bright and talkative. He said he had no aches or pains. His head was freely movable. There was no stiffness of the neck, and the Kernig sign was negative."

Case No. X, after one injection: "The temperature after a rise to 104.6° F. fell rapidly, reaching 100.3° F. in 24 hours. The improvement in general condition followed hand-in-hand. He became rational. His headache disappeared. The stiffness of the neck cleared up in 48 hours. In 72 hours the Kernig sign was no longer positive."

Case No. XV, on the fourth day of the disease, after the second injection: "Although the temperature fell by lysis and did not reach normal until the sixteenth day, still no more serum was injected on account of the marked improvement in the patient. His mind cleared up in 24 hours and his headache was relieved. In 48 hours, the Kernig sign and stiffness of the neck were disappearing."

Case No. XVII, after the first injection: "In 10 hours the temperature fell from 105° to 106° F. down to 101.4° F. The child was bright and apparently comfortable. The eyes were straight, but the neck still stiff."

Case No. XIX, after the second injection: "The results were wonderful to observe. The temperature fell to 98.6° F. in 12 hours, and with it the signs and symptoms entirely disappeared. His mind was clear. His eyes were straight. No rigidity remained."

Case No. XX, after the first injection: "He became rational and said he felt better. His headache was gone. The stiff neck and bilateral Kernig sign persisted."

These quotations illustrate well the fact that the symptoms respond rapidly to the serum, clearing up as a rule in the first 12 to 24 hours, whereas the signs disappear later in the second and third days following an injection.

(1) *Headache,* present in 19 of the cases, disappeared

After 1 injection of serum in 8 of these.
After 2 injections of serum in 9 of these.
After 6 injections of serum in 1 of these.

One case, No. XXI, continued to suffer headaches even after 12 injections of serum. He had hydrocephalus.

It is not out of place to mention here that the headaches were relieved in spite of the fact that as much fluid was injected as was removed. In 12 instances the amount injected exceeded that removed. And still the headache was benefited by the procedure.

(2) *Pains* occurred in 14 of the cases.

They were general in 3 cases.
In the neck in 10 cases.
In the back in 2 cases.
In the limbs in 1 case.

In two of the cases with *general pains* the relief came from one injection of serum (Nos. X and XVIII). In Case No. XXI they persisted in paroxysms until death. In Case No. XXII the pains in the neck and back disappeared after one injection. It is striking, however, that in the rest (9 cases with pain in the neck, 1 in the back, and 1 in the legs), *two* injections were required—with the exception of Case No. XVI, where three were needed.

(3) *Hyperæsthesia,* prominent in 11 cases, disappeared after 1 injection in 6 cases, after 2 injections in 2 cases, and after 3 injections in 2 cases. It persisted until death in Case No. XXI.

(4) *Vomiting,* in 13 cases, recurred in but one instance after the first injection of serum.

(5) *Delirium* was present in 15 cases. It disappeared

After 1 injection in 8 cases.
After 2 injections in 4 cases.
After 3 injections in 1 case
In Cases Nos. XIII and XXI it persisted.

(6) *Stupor.*—Five cases were dull and stupid, 4 becoming brighter after 1 injection, and 1 after 2 injections.

(7) *Convulsions* did not recur after the use of serum, except in the 2 cases, Nos. IV and VII, which died. They also remained *unconscious.* Two cases came out of *coma* after 1 and 2 injections of serum, respectively.

To *summarize* the individual symptoms: The delirium, stupor, vomiting, and hyperæsthesia cleared up usually after 1 injection of serum; the headache responded to 1 injection in only one-half of the cases, requiring 2 in the others; the pains in the neck as a rule required 2 injections. When the symptoms began to clear it was with great rapidity—in 3 to 12 or 24 hours.

3. Signs. It is difficult to discuss the effect of the serum upon the symptoms of the disease apart from that upon the signs. Thus in what has preceded it has been shown that, whereas the symptoms cleared up rapidly by crisis, the signs disappeared more slowly by lysis. In nearly every instance they persisted 2 or 3 days longer than the symptoms.

The most important signs for consideration are the stiff neck, retracted head, arched back, and Kernig sign, all of them signs of muscle rigidity. The leucocytes in the circulating blood must be included but the herpes and strabismus one would not expect to be influenced.

(a) *Physical Muscular Rigidity.*—Quotations from the histories show the relation of signs to symptoms:

Case No. III, after the second injection: "During the next 24 hours the improvement was great. He became rational and recognized his family. Some headache, some stiffness of the neck, and a positive Kernig sign persisted."

After the third injection: "His condition was better each day. The Kernig was the only sign persisting."

Case No. VI, after the second injection: "A marked improvement quickly followed. All pain and rigidity disappeared in 24 hours. The Kernig sign became negative in four days."

Case No. VIII, after the second injection: "Twelve hours later his headache had disappeared and his mind was clear. But the retracted head, stiff neck, and arched back persisted."

After the third injection: "The improvement following was rapid. In two days his head and back were relaxed and the Kernig sign could hardly be called positive."

Case No. IX, after the first injection: "After a rise to 106° F. in two hours, the temperature fell rapidly, reaching normal nine hours after the injection. The mind cleared up, and the improvement was striking. Slight stiffness of the neck and a double Kernig remained after 24 hours."

After the third injection: "The temperature dropped to 100° F., but the stiff neck and positive Kernig sign remained unchanged."

After the sixth injection: "The improvement in the next 48 hours was marked. From stupor, he became bright and talkative. He said he had no aches and pains. His head was freely movable. There was no stiffness of the neck and the Kernig sign was negative."

Case No. X, after one injection: "The improvement in the general condition followed the rapid drop in temperature. He became rational. His headache disappeared. The stiffness of the neck cleared up in 48 hours. In 72 hours the Kernig sign was no longer positive."

Case No. XI, after the first injection: "The patient became rational and wanted to go home. Though less marked, his head was still retracted and the neck stiff in 24 hours. The Kernig sign was still present."

After the second injection: "Twenty-four hours later the temperature reached normal. The head was not retracted, but was movable actively or passively without pain. The Kernig sign was still present. Every other sign and symptom had disappeared. In the next 24 hours the Kernig sign had disappeared."

Case No. XII, after the second injection: "The symptoms cleared up in 48 hours. He became rational gradually and slept a good deal. General hypersensitiveness, retracted head, and stiff neck persisted 36 hours. The Kernig sign disappeared in 60 hours."

Case No. XV, after the second injection: "His mind cleared in 24 hours, and his headache was relieved. In 48 hours, the Kernig sign and stiffness of the neck were disappearing."

Case No. XX, after the first injection: "He became rational and said he felt better. His headache was gone. The stiff neck and bilateral Kernig sign persisted."

After the second injection: "The temperature fell to normal in 24 hours and remained there. However, it was two days before the rigid neck and Kernig sign disappeared."

These quotations show that it is almost the rule to have the signs disappear later than the symptoms, and the Kernig is the last of them all to go.

TABLE NO. XXXIX.—NUMBER OF INJECTIONS NEEDED TO CAUSE DISAPPEARANCE OF SIGNS.

| After | 1st injection. | 2d injection. | 3d injection. | 6th injection. |
|---|---|---|---|---|
| Stiff neck cleared in | 5 cases | 7 cases. | 5 cases. | 1 case. |
| Retracted head " | " 3 " | 2 " | 2 " | |
| Arched back " | " 3 " | 1 " | 2 " | |
| Kernig sign " | " 3 " | 5 " | 4 " | 1 " |

TABLE NO. XL.—COMPARISON OF STIFF NECK AND KERNIG SIGN.

| Case No. | The stiff neck disappeared in | The Kernig sign disappeared in |
|---|---|---|
| II. | 48 hrs. after 2d injection; | 48 hrs. after 2d injection. |
| III. | 24 " " 3d " | |
| V. | 48 " " 3d " | |
| VI. | 24 " " 1st " | 96 " " 3d " |
| VIII. | 48 " " 3d " | 48 " " 3d " |
| IX. | 48 " " 6th " | 48 " " 6th " |
| X. | 48 " " 1st " | 72 " " 1st " |
| XI. | 24 " " 2d " | 48 " " 2d " |
| XII. | 36 " " 2d " | 60 " " 2d " |
| XV. | 48 " " 2d " | 48 " " 2d " |
| XVI. | 24 " " 3d " | 24 " " 3d " |
| XVIII. | 13 " " 1st " | 13 " " 1st " |
| XX. | 48 " " 2d " | 48 " " 2d " |
| XXII. | 24 " " 1st " | 24 " " 1st " |

It usually took the same number of injections to cause the disappearance of all the signs. But they differ in the length of time they persist after the final injection. The retracted head and arched back disappear first: then the stiff neck becomes relaxed; and finally a Kernig sign is no longer obtained. (See Table XL, p. 452.)

By this table the Kernig sign is seen to have disappeared simultaneously with the stiffness of the neck in 7 instances, and, on the other hand, to have lasted as much as 72 hours longer than the latter in one case. On the average, the stiffness of the neck disappeared in 35 hours after the last injection; the Kernig sign in 50 hours.

(b) *The Blood.*—The constant presence of a polymorphonuclear neutrophilic leucocytosis has already been discussed.

The lowest count was 12,080 per cmm.
The highest count was 45,000 per cmm.
The average count was 30,000 per cmm.
4 cases had less than 20,000 per cmm.
17 cases had more than 20,000 per cmm.
11 cases had more than 30,000 per cmm.

The effect of the serum upon the leucocytes is interesting. Of the 4 cases with counts below 20,000, Nos. XI and XXII were mild.

TABLE No. XLI.—INFLUENCE OF SERUM ON LEUCOCYTES—LOW COUNTS AND MILD CASES.

| Case No. | Before serum. | After serum. |
|---|---|---|
| XI. | 16,400 | 9,000—24 hrs. after 2d injection. |
| XXII. | 16,300 | 16,200—18 " " 1st " |

In both the leucocytes fell with the improvement.

The other 2 cases were men with poor resistance.

TABLE No. XLII.—INFLUENCE ON LEUCOCYTES—LOW COUNTS AND POOR RESISTANCE.

| Case No. | Before serum. | After serum. |
|---|---|---|
| XVI. | 12,080 | 23,000—20 hrs after 1st injection. |
| | | 31,200—24 " " 2d " |
| | | 6,000— 8 dys. " 4th " |
| XXI. | 13,000 | 22,500—24 hrs. " 1st " |
| | | 17,200—36 " " 2d " |
| | | 14,800—24 " " 3d " |
| | | 11,200— 2 dys. " 4th " |
| | | 6,440 - 3 " " 5th " |

Both of these reacted to the serum by a marked increase in the

circulating leucocytes. In Case No. XVI there was not only an increase of 11,000 after the first injection, but one of 8000 more after the second. Then came the fall with improvement. It is noteworthy that there was no sign of improvement clinically after the first injection. The increase in Case No. XXI, of 9500, was due to the first injection. Improvement did not follow clinically with the subsequent fall on account of the hydrocephalus, but the spinal fluid cleared up and was rendered sterile.

Indeed, it is this relation of the leucocytes in the circulating blood to those in the spinal fluid which is interesting and will be discussed later under "Spinal Fluid."

TABLE NO. XLIII.—INFLUENCE ON LEUCOCYTES—FATAL CASES

| Case No. | Before serum. | After serum. |
|---|---|---|
| IV. | 45,000 | 52,800— |
| VII. | 24,000 | 16,400—12 hrs. after 1st injection. |
| | | 18,000—14 " " 3d " |
| | | 14,200—36 " " 3d " |
| XIII. | 36,080 | 24,600— 5 " " 2d " |
| XXI. | See above, Table No. XLII. | |

Of the fatal cases, No. XXI was discussed above. Case No. IV died of respiratory paralysis, after showing some clinical improvement. Case No. VII, fulminant, uninfluenced clinically by serum, showed a drop of 10,000 in the leucocyte count. A fall of 12,000 followed the injection of serum in Case No. XIII. At this stage complicating pneumonia developed.

TABLE NO. XLIV.—INFLUENCE ON LEUCOCYTES—COMPLICATED CASES.

| Case No. | Before serum. | After serum. |
|---|---|---|
| XIII. | 36,080 | 24,600— 5 hrs. after 2d injection. |
| XIV. | 32,600 | 27,400—24 " " 1st " |
| | | 15,000—12 " " 2d " |
| | | 13,600 24 " " 4th " |
| XVII. | 40,400 | 30,400—10 " " 1st " |

All 3 of these cases were complicated by pneumonia, but not all at the time of the preliminary drop of 5000 to 12,000. That was entirely dependent upon lumbar puncture and injection of serum.

The uncomplicated cases which recovered number 16. Three of

these had counts below 20,000 and are recorded above. The other 13 are shown in the following table:

TABLE No. XLV.—INFLUENCE ON LEUCOCYTES—HIGH COUNTS AND SEVERE CASES.

| Case No. | Before serum. | After serum. | Final. |
|---|---|---|---|
| II. | 30,000 | 15,600—24 hrs. after 1st injection. | 8,000—7 dys. after 3d inj. |
| | 37,600 | 20,400—48 " " 2d " | |
| III. | 24,000 | 18,400—48 " " 1st " | See "flare-up" below. |
| V. | 40,800 | 38,200—24 " " 1st " | 8,600—9 dys. after 3d inj. |
| | | 42,400—24 " " 3d " | |
| | | 18,200—72 " " 3d " | |
| VI. | 24,600 | 17,800—24 " " 2d " | 11,600—3 " " 3d " |
| VIII. | 23,400 | 15,200—12 " " 1st " | 3,760—19 " " 3d " |
| | | 14,400—12 " " 2d " | |
| | | 10,740—48 " " 3d " | |
| IX. | 30,000 | 29,000—24 " " 1st " | See "flare-up" below. |
| | | 26,600—24 " " 2d " | |
| | | 16,200—48 " " 3d " | |
| X. | 26,800 | 19,600—24 " " 1st " | 9,800—5 dys. after 1st inj. |
| XII. | 43,000 | 27,600—10 " " 1st " | |
| XV. | 40,600 | 31,200—17 " " 1st " | |
| | | 13,400—48 " " 2d " | |
| XVIII. | | 16,000—15 " " 1st " | 6,400—2 " " 2d " |
| | | 9,200—12 " " 2d " | |
| XIX. | 35,600 | 25,200—15 " " 1st " | |
| | | 13,200—12 " " 2d " | |
| XX. | 44,000 | 26,400—24 " " 1st " | 10,800—6 " " 2d " |
| XXIII. | 25,000 | 14,000—48 " " 1st " | |

This influence amounts to a drop in leucocytes in every case after injection of serum, and is in keeping with the change in the spinal fluid where the cell content is increased constantly by the first injection of serum.

This fall in the circulating leucocytes after the first injection has varied between 1000 and 22,000 cells to the cubic millimeter, an average of 9750, the count being made as a rule 24 hours after the injection. This rapid fall continued until a certain level was reached, after which the change to normal became gradual. This level averaged 17,560 cells, with limits of 9200 and 27,600. In 8 cases it was reached after the first injection of serum, but 4 cases required 2 injections and 1 case 3.

Three cases had reactions in the character of relapses, although in only one had the spinal fluid been sterile previous to the flare-up (No. XVI).

TABLE NO. XLVI.—INFLUENCE ON LEUCOCYTES—FLARE-UP.

| Case No. | Before serum. | After serum. |
|---|---|---|
| III. | 24,000 | 18,400—48 hrs. after 1st injection. |
| | | 23,600—before 4th injection. |
| | | 36,000— " 6th " |
| | | 13,600—48 hrs. after 6th injection. |
| | | 12,000—on discharge. |
| IX. | 30,000 | 29,000—24 hrs. after 1st injection. |
| | | 26,600—24 " " 2d " |
| | | 16,200—48 " " 3d " |
| | | 26,400—before 5th injection. |
| | | 46,000—24 hrs. after 5th injection. |
| | | 10,800— 2 wks. " 6th " |
| XVI. | 12,080 | 23,200—20 hrs. " 1st " |
| | | 31,200—24 " " 2d " |
| | | 22,000— 5 dys. " 3d " |
| | | 18,400— 8 " " 3d " |
| | | 6,000— 8 " " 4th " |

In Cases Nos. III and IX this was marked by a secondary rise in leucocytes—in No. III from 18,400 to 36,000, and in No. IX from 16,200 to 46,000. These are very well-marked rises in both cases. In Case No. III the growth of meningococci from the spinal fluid had been reduced from "250 colonies" to "2 colonies per tube." The flare-up was marked by an increase to "80 to 100 colonies per tube," a rise in temperature, and the return of headache, pain in the neck, and retraction of the head. This condition cleared up after but one more injection of serum, however, and the leucocytes fell rapidly, in 48 hours, from 36,000 to 13,600.

In Case No. IX the leucocytes rose from 16,200 after the third injection to 46,000 after the fifth, an increase of 30,000. This was during the persistence of the signs of meningitis, but a constant diminution in the growth of meningococci in the spinal fluid from "a profuse growth" in the third specimen to "6 colonies per tube" in the sixth. An acute fibrinous pleurisy may possibly be held accountable for the increase in leucocytes.

In Case No. XVI, a man of poor resistance, the leucocytes were increased by 2 injections of serum from 12,080 to 31,000. The cultures yielded "a heavy, diffuse growth" of organisms in the first specimen and "remained sterile" in the third specimen. The signs and symptoms entirely disappeared 24 hours after the third injection. But

2 days later began a relapse marked by daily paroxysms of chills and fever, stupor, and headache. The leucocytes varied between 18,400 and 22,000. One injection of 30 cc. of serum put a stop to it.

The final count is not of importance. It depended upon the time of the last count and the day of discharge. It varied between 3760 and 13,400, an average of 8720 cells.

To *summarize*: (1) Cases with high leucocyte counts showed marked reductions to levels which were nearly persistent—the majority after 1 injection of serum, some only after 2 and 3 injections. The return to normal from these levels was slow and uninfluenced by serum.

(2) In relapses or flare-ups the leucocytes were increased, and they reacted to the use of serum as in the original attack.

(3) Cases with poor resistance and low counts responded to the use of serum by an increase in the leucocytes, even doubling and tripling the original counts.

LABORATORY.

4. Spinal Fluid.—The spinal fluid in each case was studied in a uniform manner so that comparisons might be reliable. It was collected in sterile graduate cylinders and taken immediately to the bacteriological laboratory before clotting or much sedimentation had occurred. At first cell counts were made with a Thoma-Zeiss blood counter, but the infectiousness of the material and the difficulty of sterilizing the instruments without injuring them led to the adoption of a less accurate method, namely:

(a) The naked eye description of the cloudiness of the fluid, with an especial note on the comparison with previous specimens.

(b) Substantiation of this estimate of the cell content by the microscopic examination of a stained smear of the centrifugalized sediment of approximately the same amount and same extent of smear.

This showed definitely those changes in the cell content which were great enough to be of importance. The microscopical examination of the fluid before centrifugalization determined whether the cloudiness was cellular or not. It proved cellular in every case.

A portion of the fluid was centrifugalized, the same amount always, if possible, at moderate speed, for 15 minutes. This did not break up the cells. The supernatant fluid was poured off and the sediment used for cultures first. After the culture, smears were made and stained with alkaline methylene blue or Hastings' stain for an esti-

mation not only of the numbers, character, and distribution of the organisms, but also of the differential percentages of the cells. In these smears also approximately the same amount of sediment was spread by means of a uniform loop over approximately the same extent, to allow comparison. No chemical tests were employed.

(a) *Cytological Examination.*—For the cell content, then, to recapitulate, the following observations were made:

(1) Cell count with blood counter or a description of the comparative cloudiness.

(2) Microscopical examination of a stained smear of the fluid before centrifugalization, of as nearly the same amount and extent possible in each case.

(3) Microscopical examination of stained smears of the centrifugalized sediment of as nearly the same amount and extent possible in each case.

Before an injection of serum the specimens of spinal fluid from the different cases varied greatly in character.

TABLE NO. XLVII.—CHARACTER OF SPINAL FLUID BEFORE INJECTION OF SERUM.

| Case No. | Clear. | A faint cloud. | Cloudy. | Very cloudy. | Very densely cloudy. | Bloody. |
|---|---|---|---|---|---|---|
| I. | | | + | | | |
| II. | + | | | + | | |
| III. | | | | + | | |
| IV. | + | | | | | |
| V. | | | + | | | |
| VI. | | | | + | | |
| VII. | | | | | + | |
| VIII. | | | + | | | |
| IX. | | | | | + | |
| X. | | + | | | | |
| XI. | | + | | | | |
| XII. | | | | + | | |
| XIII. | | | | + | | |
| XIV. | | | | + | | |
| XV. | | | | + | | |
| XVII. | + | | | | | |
| XVIII. | | | | + | | |
| XIX. | | | | | | + |
| XX. | | + | | | | |
| XXI. | | | | + | | |
| XXII. | | | | | + | |
| XXIII. | + | + | | | | |

In 4 cases the fluid was described as "*clear and limpid plus flocculi.*" These flocculi were numerous in Case No. II, fine and few in Cases Nos. IV, XVII, and XXIII. In No. XVII they amounted to débris only, but in No. XXIII there was a small content of cells of which polymorphonuclear leucocytes predominated. These 2 specimens were obtained on the seventh and sixth days, respectively. In Cases Nos. II and IV, observed on the forty-fourth and fourteenth days, respectively, the flocculi were small clumps of cells in which small mononuclear leucocytes predominated. A differential count of Case No. II showed small mononuclears 62 per cent, and polymorphonuclears 38 per cent. No tubercle bacilli were found in either case. They both were alike in being subacute or chronic infections. The fluid in Case No. II was very misleading. The impression that the case was tuberculous was not cleared up until a faint growth of meningococci was demonstrated several days later. Cases Nos. II and XXIII changed after lumbar puncture without serum injection, to cloudy fluids with predominating polymorphonuclear leucocytes. In Case No. XIX the fluid was "*bloody,*" and showed only a few polymorphonuclears in smears.

The other 18 cases all had cloudy fluids of varying degrees, depending upon the number of cells present. The spinal fluid was

"Slightly" or "faintly cloudy" in 3 cases.
"Cloudy" in 3 cases.
"Very cloudy" in 9 cases.
"Very densely cloudy" or "purulent" in 3 cases.

An idea of the number of cells which these objective descriptions indicate can be had from the fact that in Cases Nos. II and XVI the "very cloudy" fluids contained, respectively, 1350 and 1383 cells to the cubic millimeter. The fluid at the 3d tapping in Case No. II was "faintly cloudy" and contained 40 cells to the cubic millimeter. "Very densely cloudy" fluids in Case No. III contained 4800 and 8680 cells per cubic millimeter. A "very densely cloudy" fluid at the 2d tapping of Case No. XVI contained 412,000 cells to the cubic millimeter. In these 18 specimens of cloudy fluids, polymorphonuclear neutrophilic leucocytes predominated in every instance, with large endothelial cells and small mononuclear leucocytes in sufficient numbers to have their presence recognized.

We have already indicated that in 2 (Nos. II and XXIII) of the 4 cases with a clear spinal fluid a very definite cloud developed after simple lumbar puncture without serum injection. In both instances

TABLE NO. XLVIII. CHARACTER OF SPINAL FLUID

| Case No. | Before serum. | After 1st serum. |
|---|---|---|
| II | 48th day: Very cloudy. 1350 cells to cmm.; p.m.ns.* | 49th day: Only faintly cloudy; p.m.ns. |
| III | 3d day: Very cloudy; p.m.ns. | 5th day: More cloudy than previous; 4800 cells to cmm.; p.m.ns. |
| IV | 11th day: Clear; flocculi; few cells; s.m.ns.* | 15th day: Very cloudy; marked increase in p.m.ns., which now predominate. |
| V | 22d day: Cloudy; p.m.ns. | 23d day: More cloudy. |
| VI | 5th day: Very cloudy; p.m.ns. | 6th day: Even more cloudy; p.m.ns. |
| VII | 1st day: Very densely cloudy; p.m.ns. | 2d day: Even more cloudy; marked increase in p.m.ns. |
| VIII | 5th day: Cloudy; p.m.ns. | 6th day: More cloudy. |
| IX | 3d day: Very densely cloudy; p.m.ns. | 4th day: Even more cloudy; p.m.ns. increased. |
| X | 5th day: Faintly cloudy; p.m.ns. | Only one puncture. |
| XI | 15th day: Faintly cloudy; p.m.ns. | 16th day: Definitely more cloudy; p.m.ns. increased markedly. |
| XII | 3d day: Very cloudy; p.m.ns. | 3d day—10 hrs. later: More cloudy; extremely purulent. |
| XIII | 4th day: Very cloudy; p.m.ns. | 5th day: Extremely cloudy; increase of p.m.ns. |
| XIV | 3d day: Very cloudy; p.m.ns. | 4th day: Even more cloudy; p.m.ns. increased. |
| XV | 3d day: Very cloudy; p.m.ns. | 4th day: Quite bloody; as cloudy as previous; p.m.ns. increased. |
| XVI | 7th day: Quite cloudy; p.m.ns.; 1383 cells. | 8th day: More cloudy; p.m.ns. increased; very densely cloudy; 412,000 cells to cmm. |
| XVII | 7th day: Clear; flocculi; no cells. | 8th day: Very cloudy; p.m.ns. |
| XVIII | 3d day: Quite cloudy; p.m.ns. | 4th day: More cloudy. |
| XIX | 2d day: Bloody; only a few p.m.ns. | 2d day—15 hrs. later: Still bloody; p.m.ns. increased. |
| XX | 2d day: Faintly cloudy; a few p.m.ns. | 3d day: Quite cloudy; p.m.ns. increased. |
| XXI | See Table No. XLIX below. | |
| XXII | 6th day: Purulent; abundant p.m.ns. | (Only one puncture.) |
| XXIII | 8th day: Faintly cloudy; a few p.m.ns. | Only one puncture. |

*p.m.ns.=polymorphonuclears; s.m.ns.=small mononuclears; w.b.c.=white blood cells.

FTER SERUM — INFLUENCE UPON CELL CONTENT.

| | After 2d serum. | After 3d serum. | 4th serum. | 5th serum. |
|---|---|---|---|---|
| ..... | 51st day : Much less cloudy ; 40 cells to cmm.; p.m.ns. | | | |
| .... .... | 6th day : ..... Even more cloudy; 8880 cells p.m.ns. | 9th day : ..... Still cloudy. | 13th day ..... .... Still cloudy. | 16th day : Very cloudy ; a flare up. |
| ... .. .... | 16th day : More cloudy; p m.ns. increased. | | | |
| .... ..... | 24th day ..... Still cloudy. | 32d day : Clear; flocculi; no cells. | | |
| ..... | 2d day—9 hrs. later : .... Not so cloudy. | 3d day ..... Not so cloudy. | 3d day 9 h. later : Not so cloudy. | |
| ..... | 7th day : Less cloudy ; many flocculi dim. w.b.c.* | | | |
| ..... | 5th day : ..... ..... Still very cloudy. | 7th day : ..... Still very cloudy; Abundant p.m.ns. | 8th day : ..... ..... Less cloudy. | 10th day : Still very cloudy. |
| .... . . | 5th day—12 hrs. later : Still very cloudy; bloody toward end. | | | |
| ..... | 5th day : ..... Not so cloudy; p.m.ns. diminished. | 6th day : Mark'ly clearer. | | |
| ..... ..... | 9th day . ..... ..... Less cloudy. | 19th day : Very cloudy ; increased p. m.-ns.; flare-up. | | |
| .. .. .. | 3d day More cloudy; slightly bloody; p.m.ns. increased. | | | |

the cloud was due to an increased content of polymorphonuclear cells. In Case No. XXIII it became "slightly cloudy." Polymorphonuclear leucocytes predominated as in the first specimen. But in Case No. II, what might be called a tuberculous type of fluid, "clear with flocculi and predominating small mononuclear cells," was changed entirely to a "very cloudy" fluid, polymorphonuclears abounding (1350 per cmm.) to the almost total disappearance of mononuclears.

This complete change in the character of the spinal fluid after a simple lumbar puncture has been noticed repeatedly in the cases so treated during the last 19 years. In the past year it has been noticed in two cases of tetanus after the first intraspinal injection of magnesium sulphate. In the first of these,[27] the change caused considerable anxiety until cultures were demonstrated to be absolutely sterile.

Stress has been laid upon this phenomenon occurring when no serum is used, because it is one of the forms of reaction credited to the serum. And apparently with justice! For in every instance, notwithstanding the previous degree of cloudiness, the specimen of spinal fluid obtained after the first injection of serum, that is at the second puncture, has been more cloudy than the previous specimen, due constantly to an increase in polymorphonuclear neutrophilic leucocytes. (See Table XLVIII, pp. 460-461.)

In Case No. I the observations were not made by the author and so are not used for comparison. In 3 cases, Nos. X, XXII, and XXIII, the cases cleared satisfactorily after 1 injection of serum, and no second puncture was made. So there was no opportunity to study the effect of the serum upon the spinal fluid. Case No. XXI is recorded on the following table by itself, because of the great number of lumbar punctures (17) and of injections of serum (12).

TABLE No. XLIX. CHARACTER OF SPINAL FLUID AFTER INJECTION OF SERUM IN CASE No. XXI.

XXI. ... Before serum: 9th day—Quite cloudy: p.m.ns.*
After 1st serum: 10th day—More purulent; great increase in p.m.ns.
After 2d serum: 12th day—Less cloudy.
After 3d serum: 13th day—Much less cloudy: fewer p.m.ns. and relatively more s.m.ns.* *Non-organisms.*
After 4th serum: 16th day—Less cloudy.
After 5th serum: 19th day—Clearer than previously; mononuclear elements increasing.
After 6th serum on 20th day, and 7th serum on 27th day—Quite clear; only a few cells.
No serum given at puncture No. 8, 27th day.
At puncture No. 9, 40th day—*Organisms returned*: faintly cloudy.
After serum at No. 9, 41st day—More cloudy: p.m.ns. increased.
After serum at No. 10, 42d day—Clearing again; less p.m.ns.
After serum at No. 11, 43d day—Cloudy: p.m.ns.
After no serum at No. 12, on the 43d day—Cloudy: p.m.ns.
At 6 more punctures, serum only at No. 14, fluid remained cloudy with p.m.ns.

*p.m.ns.=polymorphonuclears; s.m.ns.=small mononuclears.

Of the remaining 19 cases, in only 1 (No. II) was the cell content not increased after the first injection of serum. And this is one of the cases described above in which the fluid originally clear with flocculi and mononuclear cells became cloudy with polymorphonuclears after simple lumbar puncture without use of serum.

TABLE No. L.—INFLUENCE OF SERUM UPON CELL CONTENT OF SPINAL FLUID.

+ = increase over preceding specimen; − = diminution; ± = no change.

| Case No. | After { | 1st serum. | 2d serum. | 3d serum. | 4th serum. | 5th serum. |
|---|---|---|---|---|---|---|
| II | | − | (no growth) | | | |
| III | | + | + | ± | ± | + |
| IV | | − | + | | | |
| V | | − | (no growth) | − | | |
| VI | | + | | | | |
| VII | | + | (heavy growth) | − | (5 colonies) | |
| VIII | | − | (no growth) | | | |
| IX | | + | (heavy growth) | − | (3 colonies) | ± |
| X | | 0 | | | | |
| XI | | + | | | | |
| XII | | − | | | | |
| XIII | | + | ± | | | |
| XIV | | + | (no growth) | − | | |
| XV | | + | | | | |
| XVI | | + | (no growth) | + | | |
| XVII | | − | | | | |
| XVIII | | + | | | | |
| XIX | | − | + | | | |
| XX | | + | | | | |
| XXI | | + | (no growth) | − | − | |
| XXII | | 0 | | | | |
| XXIII | | 0 | | | | |

In the other 18 cases, *the first injection of serum* caused an increase in the number of cells, and always of the polymorphonuclear type. The reaction, however, to succeeding injections was different.

Of the 12 to receive *2 injections,* 3 (Nos. III, IV, XIX) showed a still greater increase; in 3 (Nos. V, IX, XIII) there was no change, and 6 (Nos. II, VII, VIII, XIV, XVI, XXI) showed a definite

diminution. These last 6 are interesting because they indicate a healing process. Four of the specimens (Nos. II, VIII, XIV, XVI) gave "no growth" on culture after the 2 injections; the fifth (No. XXI) became sterile after 3 injections; and the sixth (No. VII), though fatal, showed a progressive diminution from a "profuse growth" before the injection of serum to "5 colonies per tube" after 4 injections.

After *3 injections,* No. V showed a diminution in cells, but the fluid had given "no growth" after the second. No. IX showed the first diminution in cells after *4 injections,* and the organisms were reduced from a "heavy growth" to "3 colonies per tube."

Cases Nos. XIV, VII, and XXI continued to have constantly diminishing cell contents after 3, 4, and 5 injections, respectively.

Two cases (Nos. V and VIII) were tapped late in the course, when the process was "healing," and the fluids obtained were both of them clear, with flocculi, and few or no cells.

No. III showed no diminution in cells even after *5 injections.* In fact, at the time of the *sixth injection* the cells and organisms were very much increased—a flare-up. None the less an abrupt recovery followed the sixth injection.

This type of *flare-up,* with increased cell and bacterial content, occurred also in No. XVI after 3 injections, with recovery by crisis after the fourth. In Case No. XXI (Table No. XLIX) the fluid became quite clear after the sixth and seventh injections, and had been sterile since the third. The serum was omitted for the first time at the eighth puncture, and on the ninth the fluid was cloudy again and organisms were cultivated—a third instance of flare-up.

It was very common to have specimens colored yellowish by the serum injected at the preceding puncture, but in 3 cases, Nos. XIII, XV, and XIX, the fluid was bloody. In Case No. XIII the blood appeared at the third tapping, on the fifth day, when 19 cc. were removed. In all probability this was fluid from the cerebral spaces, inasmuch as it appeared toward the end of the flow, and a hæmorrhagic encephalitis was found at autopsy the next day. In No. XV blood was seen at the second tapping, coming early in the flow, and was probably due to trauma of the vascular membranes, inasmuch as the patient was very restive. At 3 punctures in No. XIX, at 15-hour intervals, the fluid was bloody. There was no reason for more than ordinary trauma,

and the specimens suggested a hæmorrhagic exudate. The case recovered.

We have already described the 4 cases with clear spinal fluid plus flocculi before the injection of serum. These flocculi, few in number and small, were only seen with difficulty after shaking, although there was no visible sediment. They suggested little cotton fibers from the plug in the graduate. In 2 of the cases the fluid became cloudy after simple puncture; in the other 2 (Nos. IV and XVII), it was after the use of serum that this clear, tuberculous-like, mononuclear-containing fluid became clouded by the outpouring of polymorphonuclear leucocytes.

This same effect is shown in a more striking manner in the following cases of tuberculous meningitis. We felt we had no right to attempt to treat these cases with Flexner's serum, but the first injection was always given when there was a shade of doubt as to the type of meningitis.

Case A.—Hospital No. 63,601. Tuberculous meningitis; death.

V. W., male, negro, æt. 5 months, was admitted in the tenth week of the disease. The leucocytes were 29,200 with small mononuclears predominating.

*Lumbar Puncture No. 1* was done at once.

| | |
|---|---|
| Pressure | 460 mm. |
| Fluid removed | 30 cc. |
| Antimeningitis serum injected | 15 cc. |

The fluid was clear with fine flocculi which microscopically were composed of small mononuclear leucocytes and a few polymorphonuclears. The next day the leucocytes in the circulating blood were 18,800 and polymorphonuclears instead of small mononuclears predominated. 53 cc. of spinal fluid were removed, under a pressure of 300 mm. And the fluid now, in 24 hours, had become very cloudy. Polymorphonuclears abounded almost to the exclusion of any other cell. And *B. tuberculosis* was demonstrated in smears. Cultures from both tappings were negative. The course of the disease was uninfluenced apparently.

Case B.—Hospital No. 63,261. Acute miliary tuberculosis; tuberculous meningitis; death.

A. B., male, negro, æt. 2 years, was admitted on the twenty-sixth day of the disease. The leucocytes were 26,600, with small mononuclears predominating.

*Lumbar Puncture No. 1* was done at once.

| | |
|---|---|
| Pressure | 310 mm. |
| Fluid removed | 17½ cc. |
| Antimeningitis serum injected | 15 cc. |

The fluid was clear and limpid. Small mononuclear leucocytes were present in fair numbers. No tubercle bacilli were found. Cultures were negative.

The next day the leucocytes were 42,400 with proportionately more polymorphonuclears. 17 cc. of spinal fluid were removed, under 250 mm. pressure. The change was remarkable. The fluid was very cloudy and contained only a few small mononuclear leucocytes and large endothelial cells compared to the great number of polymorphonuclears. *B. tuberculosis* was now easily demonstrated almost entirely within cells. However, there was no evidence that the general condition was influenced in any way.

Case C.—Hospital No. 63,262. Acute miliary tuberculosis. Acute tuberculous meningitis; acute broncho-pneumonia; death.

E. B., male, negro, æt. 4 years, a brother of Case B, was admitted in the fourth week of the disease. The leucocytes were 20,800, small mononuclears predominating.

*Lumbar Puncture No. 1* was done at once.

| | |
|---|---|
| Pressure | 300 mm. |
| Fluid removed | 31 cc. |
| Antimeningitis serum injected | 15 cc. |

The fluid was clear and limpid, containing many small mononuclear leucocytes, but no tubercle bacilli. Cultures were negative.

The next day 40 cc. of spinal fluid were removed under a pressure of 600 mm. The fluid had become definitely cloudy. Polymorphonuclear leucocytes were present now in considerable numbers, but small mononuclears still predominated. No tubercle bacilli were found. The circulating leucocytes rose to 38,400 and showed a predominance of polymorphonuclears. No other effect of the serum was apparent.

Case D.—Hospital No. 62,767. Pulmonary tuberculosis; tuberculous meningitis; discharged.

M. W., negress, æt. 16 months, was admitted in the fourth week of the disease. The leucocytes were 16,000, polymorphonuclears predominating.

*Lumbar Puncture No. 1* was done at once.

| | |
|---|---|
| Pressure | 460 mm. |
| Fluid removed | 42 cc. |
| Antimeningitis serum injected | 15 cc. |

The fluid showed a very faint cloud and great numbers of fine flocculi.

The cells were 67 per cent small mononuclears, 25 per cent polymorphonuclears, and 8 per cent endothelial cells. *B. tuberculosis* was present in clumps and was cultivated in 3 weeks upon glycerine agar.

The next day the leucocytes were 22,200, polymorphonuclears predominating. 48 cc. of spinal fluid were removed under 420 mm. pressure. The fluid was much more cloudy. Small mononuclear leucocytes had almost entirely disappeared and there was a great increase in polymorphonuclears. *B. tuberculosis* was easily demonstrated, but now almost entirely within the cells. Tubercle bacilli were recovered by culture. The course of the disease was not influenced.

Case E.—Hospital No. 64,635. Pulmonary tuberculosis; tuberculous meningitis; death.

A. J., male, negro, æt. 18 years, was admitted in the fourth week of the disease. The leucocytes were 6920, 88 per cent polymorphonuclears and 8 per cent small mononuclears.

*Lumbar Puncture No. 1* was done at once.

| | |
|---|---|
| Pressure | 300 mm |
| Fluid removed | 25 cc. |
| Antimeningitis serum injected | 12 cc. |

The fluid was tinged with fresh blood. No other cloud was apparent. The corrected estimate of leucocytes was 175 to the cubic millimeter, of which 85 per cent were small mononuclears and 15 per cent polymorphonuclears.

The next day the circulating leucocytes were 11,948, mainly polymorphonuclears. 35 cc. of spinal fluid were removed under 375 mm. pressure. The fluid was very cloudy, containing 775 cells per cubic millimetre, 54 per cent of which were polymorphonuclears and 46 per cent small mononuclears. No organisms were found. There was no change in the general condition.

Case F.—Hospital No. 67,987. Tuberculous meningitis; death.

M. L., a white female, æt. 2¼ years, was admitted on the eleventh day of the disease. The leucocytes were 17,500—whether polymorphonuclears or mononuclears predominated is not recorded.

*Lumbar Puncture No. 1* was done at once.

| | |
|---|---|
| Pressure | 200 mm. |
| Fluid removed | 15 cc. |
| Antimeningitis serum injected | 30 cc. |

The fluid contained many flocculi. The centrifugalized sediment was of small mononuclear leucocytes. *B. tuberculosis* was recovered by culture.

The next day 20 cc. of spinal fluid were removed under 400 mm. pressure. The fluid was cloudy with an increased cell content, 50 per cent of which were polymorphonuclear leucocytes. No organisms were found.

A *summary* of the noteworthy features is found in the following tables:

TABLE NO LI.—INFLUENCE OF SERUM UPON SPINAL FLUID OF TUBERCULOUS MENINGITIS.

| Case. | Before injection of serum. | | | |
|---|---|---|---|---|
| | Character. | S.m.ns.* | P.m.ns.* | T. B.* |
| A | clear; flocculi. | predominate. | few. | none. |
| B | clear. | predominate. | very few. | none. |
| C | clear. | many. | none. | none. |
| D | very faint cloud; many flocculi. | 67% | 25% | + in smears and culture. |
| E | not cloudy; blood tinged; 175 cells to cmm. | 85% | 15% | none. |
| F | flocculi; small. | many. | none. | + by culture. |
| | After injection of serum. | | | |
| | Character. | s.m.ns. | p.m.ns. | T. B. |
| A | very cloudy. | very few. | great increase. | + in smears. |
| B | very cloudy. | very few. | great increase. | + in smears; all in cells. |
| C | definitely cloudy. | still predominate. | increased. | none. |
| D | much more cloudy. | disappeared. | in abundance. | + all in cells; + by culture. |
| E | very cloudy; 775 cells to cmm. | 46% | 54% | none. |
| F | clouded; cells increased. | 50% | 50% | none. |

*S.m.ns. = small mononuclears; P.m.ns. = polymorphonuclears; T.B. = Tubercle bacilli.

*In a word,* the character of the spinal fluid in 6 cases of tuberculous meningitis was changed in a remarkable way after the injection of serum. Instead of being clear with flocculi the fluids became cloudy. The change was due in every case to the attraction of great numbers of polymorphonuclear leucocytes to the spinal fluid, where in 4 cases they became the predominating cell, instead of the small mononuclears, which greatly predominated before the injection of serum. Not only were the polymorphonuclears relatively increased and the small mononuclears diminished, but the total number of cells was increased. This was accompanied by a marked change in the leucocytes of the circulating blood.

TABLE NO. LII.—INFLUENCE OF INTRASPINAL SERUM UPON CIRCULATING LEUCOCYTES IN TUBERCULOUS MENINGITIS.

| Case. | Before serum. | After serum. |
|---|---|---|
| A | 29,200—s.m.ns.* predominate. | 18,800—p.m.ns.* predominate. |
| B | 26,600— " " | 42,400— " " |
| C | 20,800— " " | 38,400— " " |
| D | 16,000—p.m.ns. " | 22,200— " " |
| E | 6,920—88% p.m.ns. 8% s.m.ns. | 11,940— " " |
| F | 17,500— (?) | (?) |

* s.m.ns. = small mononuclears; p.m.ns. = polymorphonuclears.

Five of the cases had leucocytosis. In 3 small mononuclear leucocytes predominated. Four showed an increase after serum, 1 a diminution. The 3 with small mononuclears in predominance became polymorphonuclear, so that after serum a marked polymorphonuclear leucocytosis existed in every case. It is worthy of note that the tubercle bacilli in 2 cases after serum were easy to find, and almost entirely within phagocyting cells.

In 1 case of pure influenzal meningitis, the cell content of the spinal fluid was very much increased after serum. On the other hand, no effect at all could be observed in 3 cases of pneumococcus meningitis.

Finally, what effect has this chemotaxis for polymorphonuclear leucocytes in the spinal fluid upon the leucocytes in the circulating blood?

TABLE NO. LIII.—COMPARISON OF EFFECT OF SERUM ON LEUCOCYTES IN CIRCULATING BLOOD AND IN SPINAL FLUID.

+ = increase in cells; − = diminution in cells; ± = approximately the same; S = spinal fluid; B = blood.

| Case No. | After 1st serum. | After 2d serum. | After 3d serum. | After 4th serum. | After 5th serum. | | Case No. | After 1st serum. | After 2d serum. | After 3d serum. | After 4th serum. | After 5th serum. | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| II..... | −<br>− | ±<br>− | | | | S.<br>B. | XIII.... | +<br>− | ±<br>− | | | | S.<br>B. |
| III..... | +<br>− | +<br>− | ±<br>+ | ± | +<br>+ | S.<br>B. | XIV.... | +<br>− | −<br>− | − | ± | | S.<br>B. |
| IV..... | +<br>+ | + | | | | S.<br>B. | XV.... | +<br>− | − | | | | S.<br>B. |
| V..... | +<br>± | ±<br>± | − | | | S.<br>B. | XVI.... | +<br>+ | −<br>+ | +<br>− | − | | S.<br>B. |
| VI..... | + | − | | | | S.<br>B. | XVII.... | +<br>− | | | | | S.<br>B. |
| VII..... | +<br>− | ±<br>± | ±<br>± | − | | S.<br>B. | XVIII.... | + | − | | | | S.<br>B. |
| VIII..... | +<br>− | ±<br>± | ± | | | S.<br>B. | XIX.... | +<br>− | +<br>− | | | | S.<br>B. |
| IX..... | +<br>± | ±<br>± | ±<br>± | −<br>+ | ±<br>± | S.<br>B. | XX.... | +<br>− | − | | | | S.<br>B. |
| X..... | 0<br>− | | | | | S.<br>B. | XXI.... | +<br>+ | −<br>− | −<br>− | −<br>− | −<br>− | S.<br>B. |
| XI..... | + | − | | | | S.<br>B. | XXII.... | ± | | | | | S.<br>B. |
| XII..... | +<br>− | | | | | S.<br>B. | XXIII .... | − | | | | | S.<br>B. |

TABLE NO. LIV.—CHARACTER OF PRIMARY REACTION.

| Case No. | Incr. in S. Dim. in B. | Both incr. | Both dim. | Case No. | Incr. in S. Dim. in B. | Both incr. | Both dim. |
|---|---|---|---|---|---|---|---|
| II.. | | | × | XIII. | × | | |
| III.. | × primary. | × in flare-up. | | XIV. | × | | |
| IV.. | | · | | XV. | × | | |
| V.. | × | | | XVI. | × in flare-up. | × primary. | |
| VI.. | × | | | XVII. | × | | |
| VII.. | × | | | XVIII. | × | | |
| VIII.. | × | | | XIX. | × | | |
| IX.. | × | | | XX. | × | | |
| XI.. | × | | | XXI. | | · | × |
| XII.. | × | | | | | | |

It is the primary reaction which is of importance, and this in each case plus flare-ups amounts to 21 instances for comparison. Of these 15 were of the character of an increase in the leucocytes of the spinal fluid at the expense of a diminution in the circulating blood. In 4 the leucocytes were increased simultaneously in the spinal fluid and blood; in 2 they were diminished.

(b) *Bacteriological Examination.*—The bacteriological study of the specimens of spinal fluid was made by examination of stained smears and by cultivation of the organisms:

(1) Smears.

(2) Cultures.

(1) Smears: Smears were made with the sediment centrifulgalized according to the rule given above. They were stained with Loeffler's alkaline methylene blue, Hastings' stain, and by Gram. Observations were recorded

(a) Of the presence of Gram-negative diplococci.

(b) Their number.

(c) The proportion of intracellular and extracellular forms, and

(d) Their staining properties.

Biscuit-shaped diplococci, occurring in single or double pairs, or as tetrads, and not taking the Gram stain, were demonstrated in smears of the sediment of 22 of the 24 cases at first puncture. In the other 2 they were recovered by culture. These organisms resembled each other in the different specimens and agreed morphologically and tinctorially with Weichselbaum's[28] original description of the *Diplococcus intracellularis meningitidis*. No strains were Gram-positive as Jaeger[29] described. In one case, No. XIV, it was striking that the organism oc-

curred in chains of pairs rather than in tetrads or groups. This seemed more than "accidental chain formation" (Elser and Huntoon),[30] but the characteristic was not retained in cultures. The metachromatic granules which were described by Councilman, Mallory, and Wright,[31] and Osler,[32] to which attention has recently been drawn by Elser and Huntoon,* were very commonly observed.

In only one case, No. VI, was this organism not recovered by culture as confirmation of the smears. In this instance the characteristics of the organism in smears convinced us of their identity.

The number of organisms before the injection of serum varied greatly, but after its use the result was nearly always the same, as shown in Table LV, p. 472.

The essential feature of Table LV is that, with one or two exceptions, there was a progressive diminution in the number of organisms seen after each injection of serum until they became very few and difficult to find or disappeared entirely. Much more important, of course, is the question of viability and virulence. In 17 of these instances, when they could not be recovered by culture, they could be seen in smears; and when thus seen, as is discussed in detail later, they were wholly within cells and apparently in a poor state of health, in 16 of the instances.

In Cases Nos. III and XVI the increase in number is coincident with other signs of a flare-up. The increase at the second tapping in Case No. II is after simple puncture; in Cases Nos. V and XXI, it follows the injection of serum. But the serum had apparently not produced its effect, for no organisms could be found after the third injection in Case No. V and after the fifth in Case No. XXI.

More important than the number of organisms is their distribution within or out of the leucocytes. The influence of the serum in promoting phagocytosis is more striking than the reduction of the number of organisms and is in keeping with the powerful attraction for leucocytes which the serum sets up in the spinal fluid. (See Table LVI, p. 473.)

Again the effect of the serum is seen in the progressively increasing phagocytosis with each injection until the final result in all but 3 cases was either the disappearance of extracullular forms or of both forms entirely. In 2 of these 3 cases (Nos. X and XXII) the effect of serum was not observed inasmuch as a second tapping was not neces-

* Loc. cit.

TABLE No. LV.—INFLUENCE OF SERUM ON SPINAL FLUID—NUMBER OF DIPLOCOCCI IN SMEARS OF CENTRIFUGALIZED SEDIMENT.

| Case No. | Before serum. | After 1st serum. | After 2d serum. | After 3d serum. | After 4th serum. | After 5th serum. |
|---|---|---|---|---|---|---|
| I | in great numbers. | few. | difficult to find. | | | |
| II | a few. | many. | less. | difficult to find. | | |
| III | in great numbers. | less. | hard to find. | only a few. | many. | many. |
| IV | a few. | very few. | very few. | | | |
| V | few. | many. | a few. | none. | | |
| VI | many. | a few. | | | | |
| VII | many. | less. | very few. | very few. | very few. | |
| VIII | in great numbers. | less. | very few. | | | |
| IX | in great numbers. | less. | many. | less. | only a few. | hard to find. |
| X | many. | | | | | |
| XI | a few. | very few. | | | | |
| XII | many. | hard to find. | | | | |
| XIII | few. | few. | very few. | | | |
| XIV | in great numbers. | very few. | very few. | hard to find. | | |
| XV | a few. | very few. | | | | |
| XVI | in great numbers. | a few. | none. | many. | | |
| XVII | a few. | very few. | | | | |
| XVIII | a few. | more. | | | | |
| XIX | none. | none. | none. | | | |
| XX | very few. | none. | | | | |
| XXI | a few. | many. | less. | few. | very few. | none. |
| XXII | in great numbers. | | | | | |
| XXIII | none. | none. | | | | |

TABLE No. LVI.—INFLUENCE OF SERUM UPON SPINAL FLUID—RELATIVE INTRACELLULAR AND EXTRACELLULAR DISTRIBUTION OF DIPLOCOCCI.

| Case No. | At 1st tap. | At 2d tap. | At 3d tap. | At 4th tap. | At 5th tap. | At 6th tap. |
|---|---|---|---|---|---|---|
| I | in = out.* | (?) | (?) | | | |
| II | all out. | in = out. | all in. | all in. | | |
| III | in = out. | in = out. | all in. | all in. | in = out. | all in. |
| IV | in > out. | all in. | all in. | | | |
| V | in = out. | in > out. | all in. | none. | | |
| VI | all in. | all in. | | | | |
| VII | in > out. | all in. | all in. | all in. | all in. | |
| VIII | all out. | all in. | all in. | | | |
| IX | in > out. | in > out. | in > out. | all in. | all in. | all in. |
| X | in = out. | | | | | |
| XI | in = out. | all in. | | | | |
| XII | in = out. | all in. | | | | |
| XIII | in = out. | in = out. | all in. | | | |
| XIV | in > out. | in > out. | all in. | all in. | | |
| XV | in = out. | all in. | | | | |
| XVI | in > out. | all in. | none. | in > out. | | |
| XVII | all out. | all in. | | | | |
| XVIII | in = out. | all in. | | | | |
| XIX | none. | none. | none. | | | |
| XX | all out. | none. | | | | |
| XXI | in = out. | in = out. | in > out. | all in. | all in. | none. |
| XXII | in = out. | | | | | |
| XXIII | none. | none. | | | | |

* An attempt is here made to express by the words "in" and "out" the number of intra and extracellular diplococci.

TABLE No. LVII. INFLUENCE OF SERUM UPON SPINAL FLUID. STAINING PROPERTIES OF THE DIPLOCOCCI.

| Case No. | At 1st tap. | At 2d tap. | At 3d tap. | At 4th tap. | At 5th tap. | At 6th tap. |
|---|---|---|---|---|---|---|
| I | distinct. | (?) | indistinct. | | | |
| II | distinct. | distinct. | indistinct. | indistinct. | | |
| III | distinct. | indistinct. | very indistinct. | indistinct. | distinct. | distinct. |
| IV | distinct. | indistinct. | very indistinct. | | | |
| V | distinct. | distinct. | very indistinct. | none. | | |
| VI | distinct. | indistinct. | | | | |
| VII | distinct. | indistinct. | very indistinct. | very indistinct. | very indistinct. | |
| VIII | distinct. | distinct. | very indistinct. | | | |
| IX | distinct. | distinct. | distinct. | very indistinct. | very indistinct. | very indistinct. |
| X | distinct. | | | | | |
| XI | distinct. | indistinct. | | | | |
| XII | distinct. | indistinct. | | | | |
| XIII | indistinct. | indistinct. | very indistinct. | | | |
| XIV | distinct. | indistinct. | very indistinct. | very indistinct. | | |
| XV | distinct. | indistinct. | | | | |
| XVI | distinct. | indistinct. | none. | distinct. | | |
| XVII | distinct. | indistinct. | | | | |
| XVIII | distinct. | indistinct. | | | | |
| XIX | none. | none. | none. | | | |
| XX | distinct. | none. | | | | |
| XXI | distinct. | distinct. | indistinct. | indistinct. | very indistinct. | none. |
| XXII | distinct. | | | | | |
| XXIII | none. | none. | | | | |

sary. The third (No. XVI) received serum during a flare-up and recovered.

Finally, records were kept of the staining properties of the diplococci —as to whether they stained deeply and distinctly, with clear-cut outlines, or poorly and were indistinct, shadowy, and apparently going to pieces. In other words, were they healthy, virulent, and viable organisms, or did they show the effect of some bactericidal influence?

In Table LVII (p. 474) the terms "distinct," "indistinct," and "very indistinct" are used for brevity and imply the comparative difference of the organisms in taking the stains. Interpreted as "*distinct*" are such descriptions as these upon the histories: "stain well," "clearly staining," "clearly defined," "stain well with clear outlines," "apparently in good health," "in a fairly healthy state." "*Indistinct*" means "poorly staining." "*Very indistinct*" is applied to the following: "indistinctly outlined," "indefinite outlines," "indistinct —a blur—going to pieces," "very poorly staining—mere shadows—disappearing."

Table LVII shows how rapidly they lose their healthy appearance after serum. Only 5 remained clearly staining after 1 injection of serum; and but 1 after 2 injections. In Cases Nos. III and XVI the organisms stained well again during the flare-ups. But in all the other cases they either became very poorly staining and hard to find or disappeared entirely.

The question arises as to whether the disappearance of extracellular forms after the injection of serum means that the organisms have become wholly intracellular. We have shown that the serum quickly renders the organisms poorly staining and indistinct. It is perfectly true that such indistinct forms outside of cells might exist, but would resemble ordinary cellular débris in smears of centrifugalized sediment. The mechanical injury of centrifugalization might render them wholly unrecognizable; whereas those in cells with the same poor staining reaction would be more likely to be detected. However, in the instances where the organisms have been described as "indistinct" and no extracellular forms seen, there have been here and there more clearly defined and better staining diplococci. "Indistinct" is the prevailing type, but not entirely so. Such a fact suggests that some extra cellular forms, did they exist, would be found in the long run by the careful examination of many slides. Particular care was always given not to injure the sediment. Furthermore, in Case No. VIII, after 1

injection of serum, the diplococci were wholly intracellular and "distinctly" stained. This was true in Case No. III, in the sixth specimen, and in Case No. VI, in the second specimen. These facts and the impression gained from study of the whole series has led us to feel that phagocytosis played an important rôle in the destruction of the organisms. The direct bactericidal power of the serum demonstrated in vitro cannot be measured clinically. It probably is the controlling factor in overcoming the infection. Is there any reason then to feel sure that the organisms within the cells are no longer formidable? Does phagocytosis mean a victory of the cells over the organisms? At any rate, in 30 instances of specimens with the organisms wholly intracellular by the smears, 16 gave "no growth" on culture, and 14 resulted in growths of 1 or 2 colonies up to 50 or more.

(2) Cultures: These were also made in as uniform a manner as possible for the sake of comparison. After centrifugalization of the spinal fluid according to the rule described above, all of the supernatant fluid was poured off. Then, with a standard platinum loop, which was reserved for this purpose alone, 2 loopfuls of the remaining sediment were smeared as evenly as possible over the surface of a tube of slanted glycerine agar. Two or more tubes were always inoculated. Human blood agar and serum were used at first, but the organisms seemed to grow as well on glycerine agar and, being transparent, it was more satisfactory in estimating the number of colonies and the amount of growth. In one instance only, Case No. XXI, specimen No. 9, did incubation of the spinal fluid result in a growth when the previous culture was negative.

The organisms in cultures were morphologically the same biscuit-shaped diplococci, which degenerated rapidly and showed involution forms. They did not take the Gram stain in any instance. The growth upon glycerine agar was of very small colonies, from a fraction of a millimeter to 2 or 3 mm. in diameter, round and clearly outlined, grayish-white, translucent, and glistening by reflected light, more easily distinguished by transmitted light. These colonies were slow growing and often required 48 hours to develop sufficiently to be discerned, if few in number. No fermentation tests were employed, and no serum reactions resorted to.

Table LVIII represents the amount of growth per tube from approximately the same amount of centrifugalized sediment of the spinal fluid. The powerful bactericidal effect of the serum is clearly demon-

TABLE NO. LVIII.—INFLUENCE OF SERUM UPON SPINAL FLUID—AMOUNT OF GROWTH OF DIPLOCOCCI.

| Case No. | Before serum. | After 1st serum. | After 2d serum. | After 3d serum. | After 4th serum. | After 5th serum. |
|---|---|---|---|---|---|---|
| I | profuse. | scant. | very scant. | | | |
| II | very scant. | 5 colonies. | no growth. | no growth. | | |
| III | 250 colonies. | 3 colonies. | 2 colonies. | 2 colonies. | 80-100 colonies. | profuse. |
| IV | 4 colonies. | 2 colonies. | no growth. | | | |
| V | profuse. | profuse. | no growth. | no growth. | | |
| VI | no growth. | no growth. | | | | |
| VII | profuse. | 50 colonies. | profuse. | profuse. | 5 colonies. | |
| VIII | 200-300 colonies. | 3 colonies. | no growth. | | | |
| IX | profuse. | profuse. | profuse. | less. | 3 colonies. | 6 colonies. |
| X | 20 colonies. | | | | | |
| XI | 3 colonies. | no growth. | | | | |
| XII | 100 colonies. | no growth. | | | | |
| XIII | 200 colonies. | 7-9 colonies. | 0-1 colonies. | | | |
| XIV | 76 colonies. | no growth. | no growth. | no growth. | | |
| XV | 25-50 colonies. | no growth. | | | | |
| XVI | profuse. | 6 colonies. | no growth. | 1-2 colonies. | | |
| XVII | 1 colony. | no growth. | | | | |
| XVIII | 2 colonies. | no growth. | | | | |
| XIX | profuse. | no growth. | no growth. | | | |
| XX | faint. | no growth. | | | | |
| XXI | 2 colonies. | profuse. | 30 colonies. | no growth. | no growth. | no growth. |
| XXII | 18 colonies. | | | | | |
| XXIII | 3 colonies. | | | | | |

strated. In 10 cases the spinal fluid became sterile after a single injection. In 3 cases only 1 puncture was done. Five of the remaining 13 gave no growth after the second injection. Two cases required 6 injections. With the flare-up in Case No. XVI, cultures again became positive. In Case No. III the number of colonies was greatly increased. It has already been pointed out that in one Case No. VI, no organisms were recovered, but the smears of the spinal fluid confirmed the clinical diagnosis.

Four cases terminated fatally—Nos. IV, VII, XIII, and XXI. Case No. IV received serum first on the fourteenth day, when he was unconscious, having convulsions and Cheyne-Stokes' respirations. After 2 injections he made a very definite improvement in general condition, but died of a respiratory paralysis on the sixteenth day. In spite of the fatal outcome the spinal fluid had already been rendered sterile. In Case No. VII, the fulminant case with repeated convulsions, the number of organisms were reduced from "a profuse growth" to "5 colonies per tube." In Case No. XIII there were "200 colonies per tube" before serum and "1 colony in 1 tube, none in the other," after 2 injections. She had a complicating bronchopneumonia and myocarditis. The spinal fluid of Case No. XXI was sterile after 3 injections. A few organisms reappeared in the ninth tapping. He had a hydrocephalus which accounted for his death. (See Section II, 7.)

## VI. Protocols and Temperature Charts.

Case No. I.—Hospital No. 59,958.

*Cerebrospinal meningitis (epidemic); chronic; 2 injections of serum, 15 cc. each; abrupt recovery; no sequelæ.*

E. F., female, white, æt. 36, was a patient of Dr. Harvey Cushing, and of special interest as the first case in which the serum was used in the Johns Hopkins Hospital. Added to this is the fact that she was the most chronic case in the series.

The onset was 8 weeks before admission, very sudden in character, with a chill, high fever, headache, nausea, and vomiting. On the 3d day she became unconscious, with stiff neck and arched back, from which she could not be aroused for 1 week. The fever gradually fell, her symptoms disappeared, and she remained in fair health until 12 days before admission, the 42d day of the disease. At this time she was suddenly taken with an attack of chilly sensations, followed by fever, headache, nausea, and some rigidity of the back. The temperature reached 103° F. and she was wildly delirious. In 12 hours she was rational and felt perfectly well again.

Four days later she suffered a similar paroxysm, and 3 others, of varying severity, followed at two- to three-day intervals. She was seen by Dr. Cushing in one of these attacks, during which he also noted the great pain, general tenderness, stiffness of the neck, nystagmus, and a coarse tremor characterizing all her movements. He performed

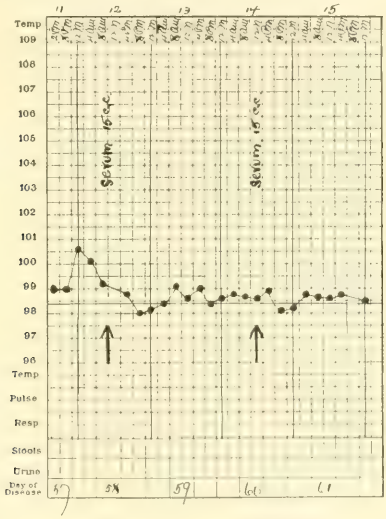



CHART No. I.—E. F. July, 1907.

*Lumbar Puncture No. 1.*

Pressure—plus.

Fluid removed—50 cc.

Antimeningitis serum injected—none.

The spinal fluid was cloudy, and contained mainly polymorphonuclear leucocytes. *Diplococcus intracellularis meningitidis* was present in great numbers, with intracellular and extracellular forms. Cultures yielded an abundant growth.

This puncture gave temporary relief to the paroxysms, but as the latter occurred repeatedly at intervals,

*Lumbar Puncture No. 2* was done upon the 58th day of the disease.

Pressure—not great.

Fluid removed—15 cc.

Antimeningitis serum injected—15 cc.

The spinal fluid was clear, and showed only a few diplococci. Cultures yielded only a scant growth.

Following this, the temperature fell rapidly to normal. She slept a great deal and was very comfortable. No more paroxysms occurred. Two days later upon the 60th day of the disease

*Lumbar Puncture No. 3* was done. A clear fluid was obtained and the injection of *antimeningitis serum* repeated. It was difficult to find organisms, and cultures yielded a very scant growth.

Her convalescence was rapid and she was discharged on the 67th day "well." A recent note states that she has had no return of the trouble—10 months after discharge.

*Discussion.*—This case is important in that the first serum received was upon the fifty-eighth day of the disease, and yet a complete cure occurred from 2 injections of the serum, 15 cc. each time.

Case No. II.—Hospital No. 62,029.

*Cerebrospinal meningitis (epidemic); chronic; 3 injections of serum (25, 20, and 20 cc.); double otitis media; recovery by lysis; no sequelæ.*

H. N., male, white, æt. 6, was a patient of Dr. W. R. Houston of Augusta, Georgia, and admitted to the hospital after 6 weeks' illness. The onset was with fever, severe headache, vomiting, stiff neck, and arched back. Pneumonia of the right lower lobe complicated the disease, lasting 10 days. Following this, after a period of normal temperature for 4 days, an intermittent type of fever began and has persisted up till admission. Daily rises of temperature to 105° F. and more, of 18 hours' duration were accompanied by severe frontal headache, rigidity of the neck and back, and general hyperæsthesia, more marked over the spine. Kernig's sign was bilaterally positive. The so-called cephalic cry was marked.

The leucocytes were 30,800, a differential count of which showed:

| | |
|---|---|
| Polymorphonuclears | 78% |
| Large mononuclears | 14% |
| Small mononuclears | 6% |
| Transitionals | 1% |
| Eosinophiles | 1% |

*Lumbar Puncture No. 1* was done on the 44th day of the disease.

Pressure—400+ mm.

Fluid removed—25 cc.

Antimeningitis serum injected—none.

The spinal fluid was clear and limpid, and contained numerous flocculi. The cell count showed

| | |
|---|---|
| Polymorphonuclears | 38% |
| Small mononuclears | 62% |

A few extracellular diplococci were seen, and cultures yielded a very scanty growth of *Diplococcus intracellularis meningitidis.*

In 24 hours the leucocytes were 37,600, but there was no change in the general condition.

At this time Dr. Bordley noted a choked disc in the left eye, and a double, subacute otitis media. Paracentesis tympani was performed in both ears, and cultures yielded a spore-bearing organism, a secondary invader of the type common to the throat.

With the diagnosis clear,

*Lumbar Puncture No. 2* was done on the 48th day of the disease.

Pressure—520 mm.
Fluid removed—35 cc.
Antimeningitis serum injected—25 cc.

The spinal fluid was very cloudy, containing 1350 cells to the cubic millimeter, mainly polymorphonuclear leucocytes. Both intracellular and extracellular diplococci were very easy to find. Two standard loops of centrifugalized sediment yielded 5 large colonies of diplococci on glycerine agar.

The temperature, which had been remittent, reached normal in 14 hours and remained 98.6° F. and below, for 10 hours, longer than at any previous time.

More marked was the change in the general condition. After a good sleep the child awoke, bright and cheerful. He noticed his surroundings for the first time and chatted about home. However, for a few hours immediately following the puncture he cried and complained of headache.

Leucocytes 15,600.

*Lumbar Puncture No. 3* was done the next day, the 49th of the disease.

Pressure—160 mm.
Fluid removed—20 cc.
Antimeningitis serum injected—20 cc.

The spinal fluid was only slightly cloudy, polymorphonuclears predominating. The diplococci were reduced in number, poorly staining, and very indistinct. They were all intracellular. Routine cultures yielded *no growth*.

It took 2 days for the temperature to reach normal after this. The headache disappeared. The leucocytes were increased to 20,400. A slight stiffness of the neck and a positive Kernig sign persisted.

*Lumbar Puncture No. 4* was done upon the 51st day of the disease.

Pressure—260 mm.
Fluid removed—20 cc.
Antimeningitis serum injected—20 cc.

The spinal fluid was much less cloudy, and contained only 40 cells to the cubic millimeter, mainly polymorphonuclear leucocytes. Diplococci were very difficult to find, and no extracellular forms were seen. Routine cultures remained sterile.

In 2 days the slight stiffness of the neck disappeared and the Kernig sign was absent. An evening rise of temperature continued for 2 weeks, never higher than 99.8° F. On the 2d day after the last injection of serum, a vesicular eruption appeared over both thighs and legs—small, scattered, discrete vesicles, which soon became pustules. Dr. Lord considered the

eruption due to the serum. The pustules yielded *Staphylococcus pyogenes albus*. A crust and brown stain remained on discharge, upon the 79th day of the disease. Aside from weakness, examination revealed nothing abnormal. His hearing was acute. A convergent squint developing upon the 58th day had disappeared. The leucocytes were 8000.

One month after discharge he was walking about, normal in all respects and showing no sequelæ.

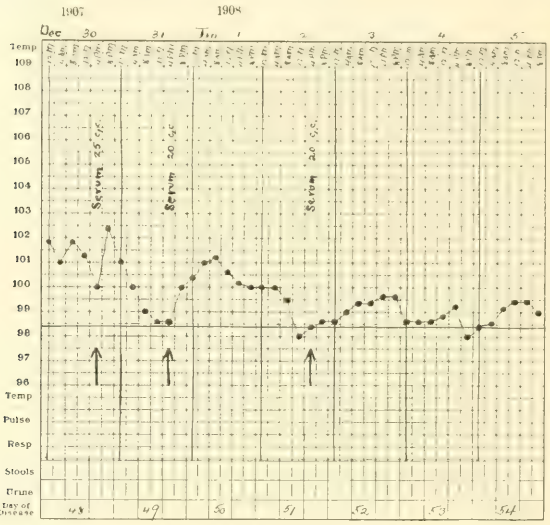



Chart No. II.—H. N.

*Discussion.*—This, the second chronic case, is of 6 weeks' duration. This and Case No. I are of special interest in that it was thought the serum would be least serviceable in chronic cases. The spinal fluid of the first puncture was clear and limpid with small flocculi; 62 per cent of the cells were small mononuclear leucocytes. In all it suggested tuberculous meningitis rather than meningococcal. It is interesting to note that the simple puncture without serum injection caused the change to the cloudy spinal fluid with large cell content, polymorphonuclear leucocytes predominating, which was found at

the second puncture. The temperature chart in this case shows the immediate fall following the serum, but the general average indicates a clearing by lysis. Each injection caused a temporary rise and then a fall. A normal temperature was not maintained, however, until 18 days after the third injection.

CASE III.—Hospital No. 62,103.

*Cerebrospinal meningitis (epidemic); acute; double otitis media; relapse; 6 injections of serum (14, 30, 20, 25, 30, and 30 cc.); less abrupt recovery; deafness in 1 ear as sequel.*

I. H., white, æt. 15, a clerk, was a patient of Dr. H. L. Whittle, Waverly, Md. For two weeks and a half the boy had suffered with influenza, but continued to work. Two days before entrance he went home at noon with severe frontal headache. That day he had 3 clonic convulsions involving the whole body. Rigidity, hypersensitiveness, and delirium developed with the advent of fever. A petechial eruption appeared over the entire body.

On admission to the hospital on the 3d day of the disease, he was unconscious, with head retracted and back arched. There was a divergent squint, marked hypersensitiveness, and a bilateral, positive Kernig sign. He had just been moved in an ambulance over a considerable distance, and his pulse was 160 to the minute, of very small size, and low tension.

The temperature was 103.2° F.

Leucocytes were 24,000, with polymorphonuclears predominating.

*Lumbar Puncture No. 1* was done at once, an hour after admission.

Pressure—400+ mm.
Fluid removed—20 cc.
Antimeningitis serum injected—14 cc.

The fluid was very cloudy, containing polymorphonuclear leucocytes mainly. *Diplococcus intracellularis meningitidis* was present equally inside and outside of cells, in great numbers, and staining very distinctly. The routine cultures yielded a luxuriant growth, about 250 colonies to a tube.

During the injection the pulse suddenly became irregular, rapid (220 to the minute), and difficult to feel at the wrist. The needle was immediately withdrawn. For 14 hours the patient was in a critical condition. His pulse was 200 or thereabouts; respirations 48 and irregular; and temperature 103 to 104° F.

Three days after admission, however, his pulse was 80 and of good quality, respirations 26, and temperature 100.4° F. He was still irrational, but could lie comfortably upon his back. His neck was stiff and the Kernig sign positive, but his head was not retracted and there was no opisthotonus.

The leucocytes were now 18,400.

*Lumbar Puncture No. 2* was done on the 5th day of the disease.

Pressure—520 mm.

Fluid removed—40 cc.

Antimeningitis serum injected—30 cc.

The fluid was more cloudy than previously. The polymorphonuclear leucocytes were 4800 to the cubic millimeter. The diplococci were mainly intracellular, reduced in number, and staining very indistinctly. Routine cultures yielded 3 small colonies on each tube.

During the next 24 hours the improvement was great. He became rational and recognized his family. Some headache, some stiffness of the neck, and a positive Kernig sign persisted. The temperature, however, remained elevated and

*Lumbar Puncture No. 3* was done on the 6th day of the disease.

Pressure—375 mm.

Fluid removed—20 cc.

Antimeningitis serum injected—20 cc.

The fluid was even more cloudy, containing 8680 cells to the cubic millimeter. Diplococci were very hard to find, all of them being intracellular, poorly staining, and with indefinite outline. Routine cultures showed 2 very small, feebly growing colonies.

His condition was better each day. The Kernig was the only sign persisting. The temperature average was lower each day until the 9th, when it suddenly rose to 103.4° F. from 99° F. The patient complained of severe headache, similar to the one at onset. He became irrational again.

Leucocytes were 23,600.

*Lumbar Puncture No. 4* was done on the 9th day of the disease.

Pressure—480 mm.

Fluid removed—46 cc.

Antimeningitis serum injected—25 cc.

The fluid was still cloudy, but showed only a few organisms, none of which were extracellular. Cultures yielded two colonies.

The temperature fell gradually until the 11th day, when impairment of hearing attracted attention to the ears. Dr. Bordley punctured the left tympanum, the discharge from which yielded *Staphylococcus pyogenes albus* and *Diplococcus intracellularis meningitidis*. On the 12th day the right tympanum was opened. Both ears discharged freely, and yet the temperature was 104° F., and the patient was complaining of headache and pain in the neck. This led to

*Lumbar Puncture No. 5* on the 13th day.

Pressure—490 mm.

Fluid removed—50 cc.

Antimeningitis serum injected—30 cc., during which patient complained of pain in the knees.

The fluid showed a flare-up. The diplococci were increased, both intracellular and extracellular, staining quite distinctly. Cultures gave 80 to 100 colonies per tube.

As previously, the temperature reached normal in 2 days, and the patient was more cheerful and bright. He had no symptoms and could roll from side to side in the bed—the first time since admission. But as suddenly again, on the 16th day of the disease, the temperature rose to

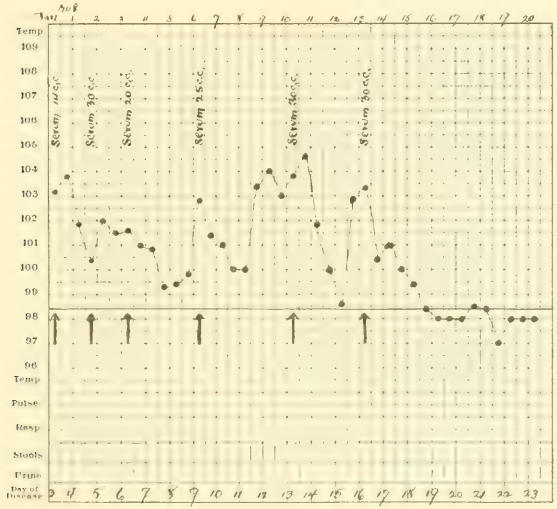



Chart No. III.—I. H.

102.7° from 98.6° F. The headache and pain in the neck returned, and the head was retracted.

Leucocytes 36,000.

*Lumbar Puncture No. 6*, on the 16th day.

Pressure—440 mm.

Fluid removed—60 cc.

Antimeningitis serum injected—30 cc., during which pain in the kness was again complained of.

The fluid was very cloudy and showed intracellular diplococci in a fairly healthy state. Cultures yielded a profuse growth.

However, this was the last injection necessary. By the 19th day, the temperature reached normal and so remained. The symptoms disappeared at once. There was no rigidity and a negative Kernig sign.

On the 24th day a divergent squint was noticed. This was present on discharge, but since then has disappeared.

The leucocytes were 13,600 2 days after the last injection and 12,000 upon discharge. Convalescence was uneventful and he was sent home in an ambulance on the 33d day, showing a normal physical condition except for

1. Divergent strabismus, and
2. Impairment of hearing in the left ear.

Three months after discharge, the deafness in the left ear was the only remnant of the attack.

*Discussion.*—We feel that if this case had received serum every day upon admission, the final result would have been gained much earlier. Evidently almost under control, a lapse in the injections, owing to attention attracted to the otitis media, allowed a flare-up.

The change after the first injection, from the very critical state he was in, was miraculous, and each time he received serum, the rapidity with which symptoms cleared up was striking. The signs were more persistent.

This patient complained very much of pain in the knees while the serum was being injected, and it lasted for several hours.

The collapse during the first injection of serum was not attributed to the injection. The patient's pulse was 160 before the operation, and of very low tension, and it was performed on admission immediately after he had been moved several miles in an ambulance.

The temperature fell to normal in about 3 days after an injection, only to rise again. The final resolution was of the less abrupt type.

CASE No. IV.—Hospital No. 62,389.

*Cerebrospinal meningitis (epidemic); acute; 2 injections of serum, 15 and 30 cc. each; spinal fluid rendered sterile; death from respiratory paralysis; artificial respiration 16 hours, 17 minutes; autopsy (tuberculous meningitis?).*

G. F., white, male, æt. 29 months, was a patient of Dr. Futcher and sent into the hospital from Arlington, Md. The onset was with vomiting 12 days before admission. Fever, restlessness, and headache followed. Three convulsions occurred within 5 hours before admission, all general in distribution and tonic in character. On admission the temperature was 101° F., pulse 124, and the respiration 36, irregular, and occasionally

Cheyne Stokes' in type. He was unconscious and held his arms spastically. The head was retracted and neck stiff. The Kernig sign was negative. There was a polymorphonuclear leucocytosis of 45,000.

*Lumbar Puncture No. 1* was done at once, on the 14th day of the disease.

Pressure—180 mm.
Fluid removed—12 cc.
Antimeningitis serum injected—15 cc.

The fluid was clear with small flocculi, showing a small cell content, small mononuclears predominating. *Diplococcus intracellularis meningitidis* was demonstrated, few in number and mainly extracellular. Routine cultures yielded 4 small colonies per tube.

His condition remained unchanged until 12 hours later, when he suddenly ceased breathing. He resumed after artificial respiration, continuing with the Cheyne Stokes' type.

On the 15th day the condition was unimproved. Leucocytes were increased to 52,800.

*Lumbar Puncture No. 2* was done.

Pressure—450 mm.
Fluid removed—25 cc.
Antimeningitis serum injected—30 cc.

The fluid was now very cloudy, from a marked increase in polymorphonuclear leucocytes. What diplococci were seen were intracellular. Routine cultures yielded 2 colonies per tube.

As before, he stopped breathing 12 hours after the puncture, but was revived by artificial respiration. Fifteen hours after the injection a most encouraging note was made:

"Patient seems to have undergone a great change. He is breathing quietly and regularly, apparently in a natural sleep. He is lying upon his back perfectly relaxed. There is no rigidity, no strabismus, and the Kernig is negative. The temperature has dropped in 2 hours from 104.4° F. to 98.6° F."

Fifteen minutes after this he again stopped breathing, to resume control after three-quarters of an hour of artificial respiration.

However, 6 hours later, on the 16th day of the disease, the final paralysis of respiration occurred. The heart's action was good, and the general circulation excellent as long as artificial respiration was continued. For 16 hours and 17 minutes it was kept up, until the heart suddenly ceased beating. During this time every known means was employed to stimulate the respiratory center—but without response.

*Lumbar Puncture No. 3* was performed in the hope that the relief of pressure might prove beneficial.

Pressure—considerable—"spurted from needle."
Fluid removed—30 cc.
Antimeningitis serum injected—none.

This fluid was more cloudy than the previous specimen, the polymorphonuclear leucocytes being increased. The diplococci were very few in number and all intracellular.

Cultures remained sterile. The temperature was very irregular, evidently not affected by the serum.

*Autopsy* (*No. 3003*) was performed by Dr. Krause, and the

*Anatomical diagnosis* made of:

Acute epidemic cerebrospinal meningitis (spinal cord especially); encapsulated caseous nodule (left lung); patent foramen ovale.

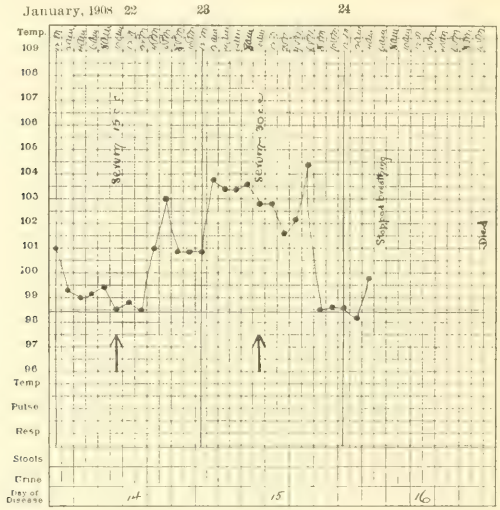



Chart No. IV.—G. F.

There was nothing of interest found aside from the changes in the nervous system, the notes upon which are:

*Brain.*—On removing the calvarium there is a gush of fluid. The brain is very soft and œdematous and has been greatly lacerated on removing it from the skull. There is no exudate anywhere on the brain, but the surface is strikingly injected. The brain immediately placed entire in formalin.

*Spinal Cord.*—The dorsal and lumbar portions of the cord were removed. On slitting up the dura it is found that the pia arachnoid is greatly dis-

tended with fluid and cells, so that it has an opaque yellowish appearance. The lining of the dura is also roughened by a fibrinous exudate in which there are abundant minute opaque whitish points which project almost like tubercles. Such minute opacities are also seen in the exudate in the pia over the cord. On tearing into this membrane, a good deal of turbid fluid runs out. The vessels of the pia are very markedly injected.

*Discussion.*—This child, the first fatal case, received his first injection of serum on the fourteenth day of the disease, when he was unconscious, having convulsions, and already showing respiratory embarrassment. Two injections, however, cleared the spinal fluid of viable organisms, for cultures from it were sterile. Like Case No. II, the clear spinal fluid with small mononuclear cells in predominance was changed to a cloudy one containing polymorphonuclears. It is a question if subcutaneous injection of the serum in addition to intraspinal might not have made use of the serum's antitoxic property and have been of avail. Smears of the nodules on the dura failed to show *B. tuberculosis,* and the microscopical examination of sections has not been made as yet by the pathologists. The presence of a caseous nodule in the lung, the finding of tubercle-like points in the dura, and the character of the spinal fluid at the first tapping are more than a suggestion of a complicating tuberculous meningitis. In the lack of absolute confirmation we shall overlook this possibility and consider it a severe case of epidemic meningitis.

Case No. V.—Hospital No. 62,554.

*Cerebrospinal meningitis (epidemic); acute; admitted on 22d day; 4 injections of serum (30, 30, 15, and 30 cc.); urticaria; blindness present on admission persisted; otitis media; recovery by lysis; general condition good on discharge.*

L. A. R., white, male, æt. 13 months, was a patient of Dr. Byrnes of Ellicott City, Md. He was brought to the hospital after 3 weeks' illness. Following an attack of influenza from which he seemed to have recovered, he was seized with vomiting suddenly upon awakening. He lost the power of his limbs, was prostrated, and had a temperature of 102° F. This fever persisted. Sixteen days before admission he had a clonic convulsion of the right side of the body, which quickly became tonic. Nine days before admission the 2d and 3d convulsions occurred. Since then the right arm and leg have been limp and useless.

On admission the eyes were open and staring, but the patient was blind. He would look up when the fingers were snapped. His hearing was good, but he evidently had no power of sight. The head was large and the anterior fontanelle bulging. The neck was stiff and the head retracted.

There was no arching of the back or Kernig's sign. Dr. Bordley noted that the eyegrounds were normal. He performed paracentesis tympani for an acute inflammation of the right middle ear, and the *B. influenzæ* and *Streptococcus pyogenes* were isolated from the pus.

The leucocytes were 40,800, mainly polymorphonuclears.

*Lumbar Puncture No. 1* was done at once, on the 22d day of the disease.

Pressure—400 mm.
Fluid removed—40 cc.
Antimeningitis serum injected—30 cc.

The fluid was cloudy with polymorphonuclear leucocytes. *Diplococcus intracellularis meningitidis* was present, both intracellular and extracellular, few in number. Routine cultures, however, yielded a profuse growth.

The injection caused the patient to cry out with pain. The fontanelle collapsed and the injection of serum did not distend it again.

The general condition remained unchanged, but the temperature fell from 101.2° to 97° F. in 2 hours.

The next day the fontanelle was tense again and leucocytes were 38,200.

*Lumbar Puncture No. 2* was done on the 23d day.

Pressure—480 mm.
Fluid removed—30 cc.
Antimeningitis serum injected—30 cc.

The fluid was more cloudy and the diplococci numerous, mainly extracellular in type. Routine cultures gave a profuse growth.

During the next 24 hours, the temperature was normal or below all the time. The patient seemed improved, sleeping soundly and taking nourishment well.

*Lumbar Puncture No. 3* was done on the 24th day of the disease.

Pressure—300 mm.
Fluid removed—62 cc.
Antimeningitis serum injected—15 cc.

The fluid was still cloudy. A few intracellular diplococci were seen, staining very poorly. Routine cultures were sterile.

Leucocytes 42,400, 24 hours later.

The improvement now was marked. The temperature rose each day, the general average getting constantly lower. In 48 hours there was no retraction of the head, no rigidity anywhere, and the hypersensitiveness had disappeared. The child began to cry and make a healthy resistance to handling.

The stare in the eyes remained and apparently he could not see at all.

Three days later, leucocytes were 18,200.

During the first week after the injection, flushes appeared at times, especially over the left cheek and ear. Urticarial wheals appeared on trunk and limbs. Although convalescence continued uninterrupted and the child gained weight and enjoyed a normal temperature, still

*Lumbar Puncture No. 4* was done on the 32d day of the disease on account of the questionable vision.

Pressure—250 mm.

Fluid removed—60 cc.

Antimeningitis serum injected—30 cc.

The fluid was clear with some small flocculi. No cells or organisms were found and the routine cultures were sterile.

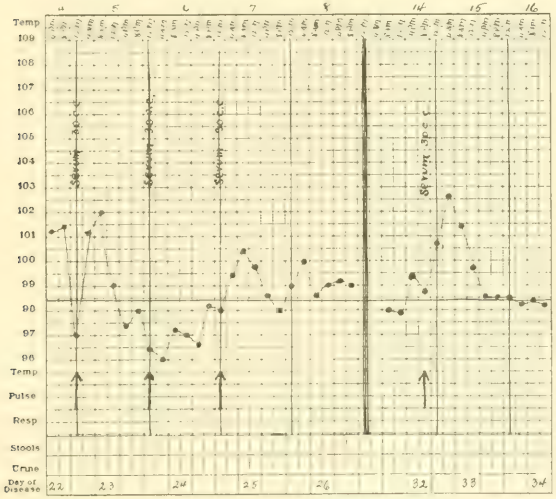



CHART NO. V.—L. A. R. February, 1908.

The reaction following the puncture and injection was marked. The temperature, which had been normal for 4 days, rose to 102.6° F. in 4 hours, and then fell gradually to normal again. The child became sleepless and irritable, the neck was a little stiff, and a strabismus appeared.

Leucocytes were 8600.

Urticarial wheals were present for several days.

On discharge, on the 54th day of the disease, Dr. Bordley noted that the child was blind. The eye grounds were normal, however. The general condition was excellent. Albumen was present in the urine 4 days before discharge.

*Discussion.*—This child was blind upon admission, on the twenty-second day of the disease. The worst sequel of the series, blindness in this case, should not rightly be credited as having occurred in spite of the serum, inasmuch as it was present before the child received serum. We must bear in mind the late date in the disease at which the patient was brought to the hospital.

The meningitis had developed after an attack of influenza, and, at least 3 weeks later, *B. influenzæ* was recovered from the middle ear.

This case required 2 injections of serum to make the spinal fluid sterile, and the symptoms and signs improved most markedly after the third. In 48 hours no sign of meningitis remained, except the blindness. The fourth puncture showed a normal fluid under slightly increased tension. The serum injected seemed unnecessary. And yet it is possible that the strabismus and slight stiffness of the neck reappearing may have been due to an explosion of toxin liberated by the bactericidal effect of the serum. The temperature chart is characteristic of the reaction following the injection of serum.

CASE No. VI.—Hospital No. 62,567.

*Cerebrospinal meningitis (epidemic); acute; 2 injections of serum, 15 cc. each; deafness, clearing before discharge; recovery by lysis; no sequelæ.*

J. G. P., white, male, æt. 23, was a patient of Dr. Hocking, Govanstown, Md. After suffering for 3 weeks with influenza—chill, fever, malaise—he was suddenly taken with an unusually severe headache 4 days before admission. He said it nearly drove him crazy. The next day the temperature was 103.5° F., he was delirious, and his neck was stiff. He was unable to swallow and vomited several times.

On admission his head was retracted. He was irrational; his pupils were unequal; his neck was stiff, and attempted motion very painful. Ecchymoses were noted on the abdominal wall. The Kernig sign was bilaterally positive.

Leucocytes were 24,000, mainly polymorphonuclears.

*Lumbar Puncture No. 1* was done at once on the 5th day of the disease.

Pressure—170 mm.
Fluid removed—17 cc.
Antimeningitis serum injected—15 cc.

The fluid was very cloudy, containing large endothelial cells and small mononuclears, but mainly polymorphonuclears. *Diplococcus intracellularis meningitidis* was present, entirely intracellular in type. Routine cultures were sterile.

During the injection the patient complained of "pain about the rectum," which was relieved immediately whenever the injection was stopped.

In 3 hours his mind was clear, and during the following 24 hours, his neck relaxed and his head could be moved. He still had a headache and pain in his back. The Kernig remained positive. A crop of herpes labialis appeared.

*Lumbar Puncture No. 2* was done on the 6th day of the disease.

Pressure—180 mm.

Fluid removed—16 cc.

Antimeningitis serum injected—15 cc.

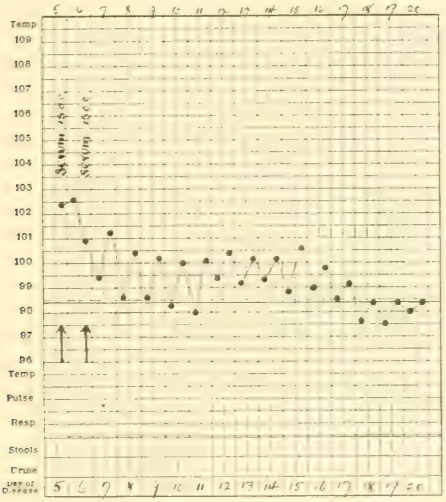



CHART No. VI.—J. G. P. February, 1908.

The fluid was even more cloudy, containing 75 per cent polymorphonuclears and 25 per cent mononuclears. A few intracellular diplococci were seen, but routine cultures remained sterile.

This injection caused him very severe pain in the hips and down the legs, which persisted for 18 hours. There was hyperæsthesia of the legs and he could not move them without the greatest pain.

A marked improvement quickly followed. All pain and rigidity disappeared in 24 hours. The Kernig sign disappeared in 4 days.

Leucocytes were 17,800 24 hours after puncture No. 2, and 11,600 3 days later.

Swollen optic discs observed on the 7th day had cleared up by the 17th. Slight deafness during the acute stage cleared before his discharge, as did a trace of albumen in the urine.

His convalescence was rapid. The temperature reached normal 11½ days after the 2d injection. On the 25th day he walked home, 20 days after admission, showing absolutely no sequelæ.

*Discussion.*—This is the only case in the series in which the organism was not recovered by culture. Smears of the spinal fluid showed only intracellular forms. He complained bitterly of the pain during the injection, more than any other case. His temperature fell by lysis in 12 days.

Case No. VII.—Hospital No. 62,810.

*Cerebrospinal meningitis (epidemic); acute; fulminant type; hemiplegia; 5 injections of serum (30, 30, 15, 30, 15 cc.); spinal fluid clearing; convulsions; death; no autopsy.*

G. H., white, male, æt. 26, was seen by Dr. Barker in consultation and sent into the hospital. Two months before admission patient had lost a child, 1 month old, from "meningitis." He himself had been drinking heavily and the onset was during a spree. Less than 24 hours before admission, while asleep, he was seized with a convulsion. A fever developed at once. He never regained consciousness.

On admission he was unconscious, breathing stertorously. There was a divergent squint, and the left eye rotated, while the right was fixed. A beginning herpes was present on the upper lip. The neck was stiff and the back arched. The Kernig sign was bilaterally positive. There was no apparent power in the right arm and leg. The left arm and leg were in constant motion. The deep reflexes were absent on the right side, and there was dorsal flexion of the right big toe to plantar stimulation.

Leucocytes were 24,000, mainly polymorphonuclears.

*Lumbar Puncture No. 1* was done on admission, on the 1st day of the disease.

Pressure—210 mm.

Fluid removed—30 cc.

Antimenigitis serum injected—30 cc.

The fluid was very densely cloudy and contained mainly polymorphonuclear leucocytes. *Diplococcus intracellularis meningitidis* was present, a clearly staining organism, more extracellular than intracellular. Routine cultures yielded a profuse growth.

The patient struggled during the injection. His condition was unchanged after the injection, the temperature, pulse, and respirations all being increased.

Leucocytes were 16,400, 12 hours after puncture No. 1.

Inasmuch as no change was noted, in 15 hours—

*Lumbar Puncture No. 2* was done.

Pressure—390 mm.
Fluid removed—35 cc.
Antimeningitis serum injected—30 cc.

The fluid was even more cloudy, there being a marked increase in polymorphonuclears. Fewer organisms were seen, all intracellular and poorly staining. Routine cultures gave 50 colonies per tube. Patient again struggled during injection.

Eight hours after injection No. 2, toward the end of the 2d day, he had 2 general clonic convulsions, lasting 1 minute each.

*Lumbar Puncture No. 3* was done 9 hours after No. 2.

Pressure—160 mm.
Fluid removed—49 cc.
Antimeningitis serum injected—15 cc.

The fluid was not so cloudy, and the only organisms seen were poorly staining, intracellular diplococci. Routine cultures gave a greater growth than previously.

Leucocytes were 18,000, 14 hours later.

His condition improved slightly. The left half of face and the right arm and leg were clearly paralyzed. He would open the right eye. The temperature was still elevated. Consequently

*Lumbar Puncture No. 4* was done 15 hours after No. 3.

Pressure—160 mm.
Fluid removed—35 cc.
Antimeningitis serum injected—30 cc.

The fluid was yellowish, not so cloudy as previously. Intracellular diplococci were seen, poorly staining. Routine cultures gave the same growth as No. 3.

In 9 hours no change was apparent and so

*Lumbar Puncture No. 5* was done.

Pressure—150 mm.
Fluid removed—30 cc.
Antimeningitis serum injected—15 cc.

The fluid was still yellow and cloudy, showing polymorphonuclear leucocytes and a few, very poorly staining, intracellular diplococci. The organisms were shadows and seemed to be disappearing. Routine cultures yielded but 5 colonies per tube.

Only a small amount of serum was injected, as the patient had a general clonic convulsion and the needle was withdrawn. The convulsion began with the eyelids and marched in order to the face, neck, arms, and legs. It passed off in the reverse order. Clonic spasms of the right arm and face persisted 17 minutes.

Two hours later the 8th convulsion occurred, of the same character,

though cut short by chloroform. The lungs were filling up and loud rhonchi were increasing. Leucocytes were 14,200.

The 4th day was a little encouraging. The pulse was irregular, of small size and low tension.

At 7.35 p. m. he had the 9th convulsion, at exactly the same time as the night before. A puncture was interrupted by the convulsion, and no fluid was obtained. Two hours later, his heart ceased beating during the 11th convulsion, an especially severe one.

The urine daily showed a heavy trace of albumen, and many hyaline and granular casts.

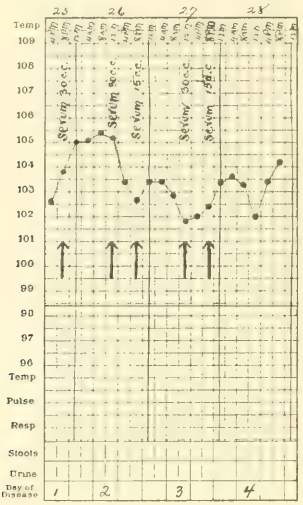



CHART No. VII.—G. H. February, 1908.

*Discussion.*—It was realized upon admission that we had a fulminant case to deal with. We felt that the serum had been ineffectual in these cases because they died before it had had time to act. So we believed that we could save this man if we were able to keep him alive at least 3 days. Heroic measures enabled us to have just 3 days in which to apply the serum. Injections were made about every 12 hours—120 cc. being given in all. The only apparent change was

in the spinal fluid itself. The organisms became intracellular, very poorly staining, and few in number. Routine cultures of the fifth tapping yielded but 5 colonies per tube.

No autopsy was allowed.

CASE No. VIII.—Hospital No. 62,748.

*Cerebrospinal meningitis (epidemic); acute; 3 injections of serum (15, 15 and 30 cc.); slight deafness; petechial eruption; acute myocarditis in convalescence; recovery by lysis; discharged well.*

C. S., male, negro, æt. 5, was brought to the hospital on the 5th day of the disease. The onset was with sudden headache and pain in the legs, after being peevish for 12 hours. He vomited upon the 1st and 2d days. The fever was noticed 3 days before admission. The day before admission the head was drawn back, and the neck and back were stiff and painful on motion.

The patient was conscious, clear mentally, and complaining that his neck was sore. The head was retracted and back arched. The Kernig sign was bilaterally positive. There was no strabismus and no herpes. Over the abdomen, back, and upper thighs was an irregular brownish mottling, suggesting the stain of a former eruption.

The fresh blood showed a polymorphonuclear leucocytosis of 23,400. Intracellular bodies resembling diplococci were seen in the fresh blood, and Hasting's and Gram stains identified them as *Gram negative diplococci.* Blood culture was negative, upon 2 successive days.

*Lumbar Puncture No. 1* was done on admission.

Pressure—400 mm.
Fluid removed—25 cc.
Antimeningitis serum injected—15 cc.

The fluid was cloudy with polymorphonuclear leucocytes. *Diplococcus intracellularis meningitidis* was present in great numbers, clear extracellular forms, staining distinctly. The absence of intracellular forms was marked. Routine cultures yielded 200 to 300 colonies per tube. Only the small amount of serum was injected because of the pain during injection, which he referred to the knees.

There was no material change during the next 24 hours. The leucocytes dropped in 12 hours to 15,200. A crop of herpes labialis appeared.

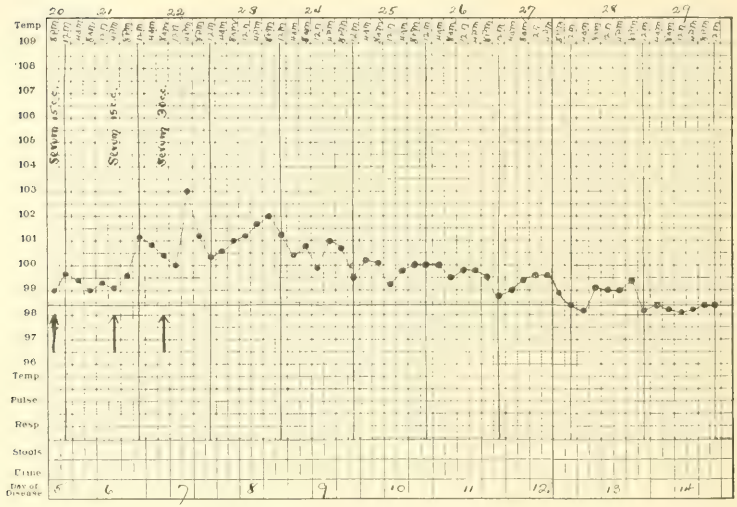
*Lumbar Puncture No. 2* was done on the 6th day.

Pressure—150 mm.
Fluid removed—15 cc.
Antimeningitis serum injected—15 cc.

The fluid was more cloudy than that of the 1st puncture. In marked contrast also were the phagocytosis and absence of extracellular diplococci. Every 15th cell contained 1 to 6 pairs of clear staining diplococci. Routine cultures yielded 3 colonies per tube.

Although the patient was under primary anæsthesia, he was roused very much by the injection. From his movements and struggles, it was judged he had pain in his legs.

Twelve hours later the leucocytes were 14,400. His headache had disappeared and his mind was clear. But the retracted head, stiff neck, and arched back persisted.




CASE No. VIII.—C. S. February, 1908.

*Lumbar Puncture No. 3* was done on the 7th day of the disease.

Pressure—210 mm.

Fluid removed—30 cc.

Antimeningitis serum injected—30 cc.

The fluid was less cloudy than previously, and it contained many fine flocculi, suggesting a healing process. The leucocytes were diminished in number and were in a poor state of preservation. No extracellular diplococci were seen, and those interpreted as intracellular were few in number and stained indistinctly as a blur, as if they were going to pieces. Routine cultures gave no growth.

Rapid improvement followed. In 2 days, his neck and back were relaxed and the Kernig sign could hardly be called positive.

Leucocytes were 10,740 on the 9th day and 3760 on the 26th.

The temperature fell by lysis and was normal on the 14th day. No signs or symtoms of meningitis were present at this time. A slight deafness in one ear had not cleared before discharge.

Then followed 5 weeks of convalescence on account of an acute myocarditis which suddenly developed. The heart was dilated and a systolic murmur appeared at the apex. Its action was extremely irregular. The murmur was present on discharge, but the heart's action seemed to be comparatively satisfactory.

*Discussion.*—The feature of this case was the marked reaction to the serum, especially in the spinal fluid. After one injection the diplococci became intracellular to the total disappearance of extracellular forms. The great reduction in the number of colonies shows their impaired viability. Two injections rendered the fluid sterile. The polymorphonuclear leucocytes were very much increased by one injection, and the drain upon the circulating blood was evidenced by a drop from 23,400 to 15,200 leucocytes in 12 hours.

The temperature, somewhat like Case No. V, was comparatively low at first, 98.6° to 99.6° F., and was raised by the serum injections to 103° F. The subsequent fall was by lysis.

The striking picture was seen of a child in opisthotonus with retracted head and stiff neck, but happy and without complaint, after two injections of serum.

Case No IX.—Hospital No. 62,867.

*Cerebrospinal meningitis (epidemic); acute; 6 injections of serum (18, 15, 30, 15, 30, 30 cc. each); persistent case; acute fibrinous pleurisy; less abrupt recovery; no sequelæ.*

I. S. H., black, male, æt. 5½ years; was a patient of Dr. Carr of Baltimore. Two days before admission he complained of feeling giddy. Two hours later, at school, he vomited. At home he was very stupid, but it was not until the next day that fever, delirium, and stiffness of the neck appeared.

On admission he was in a muttering delirium. His head was retracted and his neck stiff. The Kernig sign was bilaterally positive. There was no strabismus, or petechial eruption. There was a polymorphonuclear leucocytosis of 30,000.

*Lumbar Puncture No. 1* was done on the 3d day of the disease.

Pressure—410 mm.
Fluid removed—31 cc.
Antimeningitis serum injected—18 cc.

The fluid was very densely cloudy and showed microscopically many polymorphonuclear leucocytes, a few small mononuclears, and some large endothelial cells. *Diplococcus intracellularis meningitidis* was present, a few intracellular forms; but numerous, clear, and deeply staining extracellular groups. According to the anæsthetist the pulse and respirations were not good during the injection, and the needle was withdrawn when only 18 cc. of serum had been injected. Routine cultures yielded a profuse growth.

After a rise to 106° F. in 2 hours, the temperature fell rapidly, reaching normal 9 hours after the injection. The leucocytes remained the same—29,600. His mind cleared up and the improvement was striking. Slight stiffness of the neck and a double Kernig remained after 24 hours.

*Lumbar Puncture No. 2* was done on the 4th day of the disease.

Pressure—380 mm.
Fluid removed—24 cc.
Antimeningitis serum injected—15 cc.

The fluid seemed even more clouded with polymorphonuclear leucocytes. More cells contained diplococci and the extracellular forms were few in number. Both forms stained well, with sharp outlines. Routine cultures again yielded a heavy growth.

The temperature, which had risen again, remained elevated, 102.5° to 103.5° F. The leucocytes in 24 hours were 26,600.

*Lumbar Puncture No. 3* was done on the 5th day of the disease.

Pressure—380 mm.
Fluid removed—28 cc.
Antimeningitis serum injected—30 cc.

The fluid was still quite cloudy and showed many, clear, and distinctly staining, extracellular diplococci and very few intracellular forms. Routine cultures yielded as profuse a growth as previously. During the first 2 taps the patient was roused and disturbed by the injections. The 3d one seemed to cause no discomfort however.

The temperature dropped to 100° F., but the stiff neck and positive Kernig sign remained unchanged.

Forty-eight hours later the child was even worse, the back becoming more arched than on admission. The leucocytes were 16,200.

*Lumbar Puncture No. 4* was done on the 7th day of the disease.

Pressure—200 mm.
Fluid removed—15 cc.
Antimeningitis serum injected—15 cc.

The fluid was still extremely cloudy, with polymorphonuclear leucocytes in abundance. Only intracellular diplococci were seen and they stained very indistinctly. Routine cultures now were positive, but the growth was slight in comparison with the previous specimens. The next day the

leucocytes returned to 26,400, and the temperature, as previously, rose again after a short fall. So

*Lumbar Puncture No. 5* was done on the 8th day.

Pressure—300 mm.

Fluid removed—41 cc.

Antimeningitis serum injected—30 cc.

The fluid contained fewer leucocytes and only a few intracellular diplococci were seen. Routine cultures gave 3 colonies per tube.

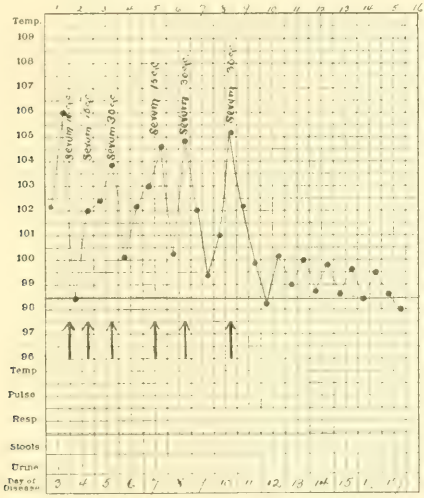



Chart No. IX.—I. S. H. March, 1908.

The 5th injection caused considerable distress. The boy squirmed and resisted, and a consequent increase in the pulse and respiratory rate occurred.

The temperature dropped and was between 99° and 100.6° F. for 12 hours the next day. However, on the 10th day it rose again, and when it reached 105.2° F.

*Lumbar Puncture No. 6* was done.

Pressure—450 mm.

Fluid removed—45 cc.

Antimeningitis serum injected—30 cc.

The fluid was still very cloudy, and an occasional intracellular diplococcus was found. Routine cultures yielded 6 colonies per tube.

The improvement in the next 48 hours was marked. The temperature fell steadily from 104.8° to 99.8° F. After being dull he became bright and talkative. He said he had no aches or pains. His head was freely movable. There was no stiffness of the neck, and the Kernig sign was negative. A slightly irregular temperature persisted, rising to about 100° F. daily, for 2 weeks. During this time he gained strength rapidly and was discharged in excellent condition on the 37th day of the disease.

A friction rub in the right lower back appeared during the fastigium while the patient was being tubbed, but it disappeared during convalescence.

The leucocytes were 46,000 before the last puncture and 10,800 2 weeks later (26th day).

*Discussion.*—This case, like Case No. III, required 6 injections of serum. The final result was a rapid clearing up, in the character of a crisis, after the sixth injection. No one of the previous injections, except the first, seemed to have any marked immediate effect. The fact that the leucocytes were higher before the sixth than at first, showed that the struggle was still on—that the process was not yet healing.

The organisms were reduced in the spinal fluid, but at no time were sterile cultures obtained.

The distress caused by the injections was striking. Even when under an anæsthetic, it was evidenced by the rapid pulse, increased respirations, and struggling. The anæsthetist learned to put the child in deepest anæsthesia just before the injection in order to avoid what at times seemed a dangerous change in pulse and respirations.

Case No. X.—Hospital No. 63,122.

*Cerebrospinal meningitis (epidemic); acute; 1 injection of serum (30 cc.); abrupt recovery; no sequelæ.*

M. G., white, male, æt. 7, was a patient of Dr. H. W. Jones, of Baltimore, Md. The onset had been 4 days previous to admission, with headache, backache, pain in the stomach, and vomiting. He soon became feverish and delirious. On admission, the neck was stiff, and attempted motion was painful. The Kernig sign was bilaterally positive; and a fresh crop of herpes had appeared at the angles of the mouth.

The blood showed a polymorphonuclear leucocytosis of 26,800.

*Lumbar Puncture No. 1* was done on admission.

Pressure—200 mm.
Fluid removed—26 cc.
Antimeningitis serum injected—30 cc.

The fluid was slightly, but diffusely cloudy, with many polymorphonuclear leucocytes, a few small mononuclears, and a few large endothelial cells. *Diplococcus intracellularis meningitidis* was present, 1 in every 50th cell. Clearly defined extracellular forms were seen. Routine cultures yielded 20 colonies per tube. The injection caused considerable pain, which was referred to the knees.

The leucocytes in 24 hours were 19,600.

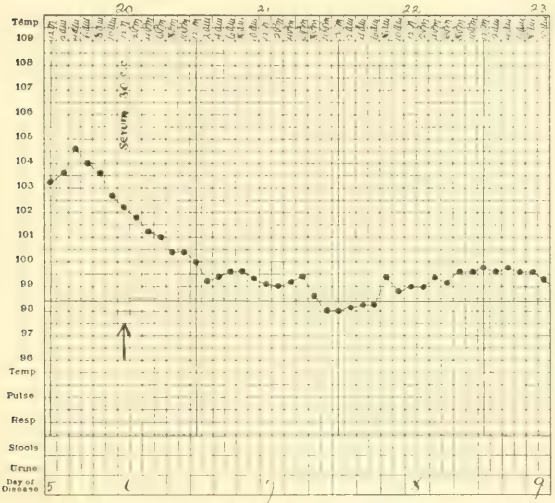



CHART No. X.—M. G. March, 1908.

The temperature, after a rise to 104.6° F., fell rapidly, reaching 99.3° F. in 24 hours. The improvement in the general condition followed hand-in-hand. He became rational. His headache disappeared. The stiffness of the neck cleared up in 48 hours. In 72 hours the Kernig sign was no longer positive.

On the 10th day of the disease the leucocytes were 9800.

On the 28th day he was discharged well, without sequelæ.

*Discussion.*—This was the first case to clear up after a single injection of serum. It was a remarkable picture of rapid fall in temperature with disappearance first of symptoms and later of signs. We

can imagine the character of the spinal fluid 24 hours after the puncture. The leucocytes in the circulating blood had fallen from 26,800 to 19,600, probably because of the demand for phagocytes in the spinal fluid. The organisms present were probably all intracellular and disintegrating. Cultures would probably have been sterile.

Case No. XI.—Hospital No. 63,149.

*Cerebrospinal meningitis (epidemic); acute; 2 injections of serum (30 and 15 cc. each); abrupt recovery; strabismus persisted.*

J. D., white, male, æt. 7, was sent in by Dr. J. H. Mason Knox, Jr. on the 14th day of the attack. The onset was sudden, at school, with headache and fever. He vomited medicine and in a few hours was delirious. Strabismus appeared early and persisted—convergent in type. Retraction of the head and stiffness of the neck caused him great pain on motion. There was no other eruption than a herpes labialis.

On admission the retraction of the head was extreme, with arching of the back. There was some general hypersensitiveness, most marked about the head and neck. A bilateral positive Kernig sign was present.

The blood showed a polymorphonuclear leucocytosis of 16,400.

*Lumbar Puncture No. 1* was done at once on the 15th day.

Pressure—210 mm.
Fluid removed—30 cc.
Antimeningitis serum injected—30 cc.

The fluid was very faintly cloudy, showing a predominance of polymorphonuclear leucocytes. *Diplococcus intracellularis meningitidis* was present in small numbers in and out of cells, staining distinctly. Routine cultures yielded 3 colonies per tube.

The temperature rose to 102.4° F. immediately following the injection, but soon fell to a level of 100° to 101° F. The patient became rational—wanted to go home. Though less marked, the head was still retracted and the neck stiff in 24 hours. The Kernig sign was still present.

*Lumbar Puncture No. 2* was done on the 16th day.

Pressure—180 mm.
Fluid removed—16 cc.
Antimeningitis serum injected—15 cc.

As during the first injection, the patient complained of pain in the back and legs and feet.

The fluid was definitely more cloudy with abundant polymorphonuclear leucocytes. Very few diplococci were seen, all intracellular and staining indistinctly. Routine cultures yielded no growth.

Twenty-four hours later, the temperature reached normal. The head was not retracted but was movable actively or passively without pain. The Kernig sign was still present. Every other sign and symptom had disappeared. Leucocytes 9000.

In the next 24 hours the Kernig sign disappeared. Dr. Mills noted at this stage a retrograde swollen disc. The slight convergent squint persisted even on discharge.

Convalescence was rapid and uneventful. He received his discharge on the 35th day, in excellent condition.

*Discussion.*—This was another case to receive serum late in the attack, when he was apparently showing no signs of improvement. The

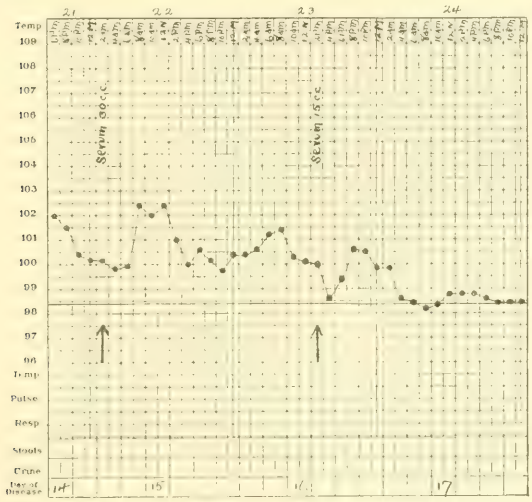



Chart No. XI.—J. D. March, 1908.

response was by crisis in temperature, symptoms, and signs. He, too, complained of pain during the injection. The temporary rise in temperature after the injections, the attraction of the leucocytes to the spinal fluid, and the diminution of their number in the circulating blood were striking features. Note that the Kernig sign persisted 24 hours after every other sign had disappeared. Again the symptoms were the first to clear. This boy was rational and quite bright in the presence of a retracted head and stiff neck.

Case No. XII.—Hospital No. 63,230.

*Cerebrospinal meningitis (epidemic); acute; 2 injections of serum (30 cc. each); suppurative otitis media; abrupt recovery; deafness as sequela.*

H. L. B., white, male, æt. 7, was admitted after an illness of 33 hours. The onset was sudden with headache and a severe chill, followed by fever. He soon became delirious. The neck was stiff and sore to the touch. Movements of the head were very painful. A general clonic convulsion had occurred 4 hours before admission.

On examination the boy was very irrational, periods of restiveness alternating with those of stupor. The neck was stiff, but no arching of the back or retraction of the head was apparent. There was no strabismus and no herpes. The Kernig sign was present on both sides. The abdominal reflexes were absent.

There was a polymorphonuclear leucocytosis of 43,400.

*Lumbar Puncture No. 1* was done on the 3d day of the attack.

Pressure—380 mm.
Fluid removed—34 cc.
Antimeningitis serum injected—30 cc.

During the injection of the first 15 cc., whenever pressure was applied to syringe, the patient would cry out, "Let me sit on the chamber."

The fluid was very cloudy with polymorphonuclear leucocytes. *Diplococcus intracellularis meningitidis* was present, not in great numbers, but staining distinctly, equally in and out of cells. Routine culture gave 100 colonies to the tube.

In 10 hours the leucocytes were 27,600.

The temperature fell to 98.8° F. but rose again to 101° F.

There was no definite improvement. The boy was irrational and resisted all attempts at care and treatment. He vomited several times.

*Lumbar Puncture No. 2* was done on the same day, 10 hours after No. 1

Pressure—200 mm.
Fluid removed—46 cc.
Antimeningitis serum injected—30 cc.

The fluid was more cloudy than previously, extremely purulent. The diplococci were hard to find, all in cells and staining indistinctly. Routine cultures yielded no growth.

In the next 24 hours the temperature did not rise above 99.2° F. But thereafter it rose varying between 99° F. and 100.7° F. for a week, until paracentesis was done to relieve an otitis media.

The symptoms, however, cleared up in 48 hours. He became rational gradually and slept a good deal. General hypersensitiveness, retracted head, and stiff neck persisted 36 hours after the 2d injection. The Kernig sign disappeared in 60 hours.

He had had a suppurative otitis media with discharge 3 months before admission, and on becoming rational he complained of pain in both ears. On the 11th day, Dr. Randolph did a paracentesis upon the right tym-

panum. Considerable discharge followed. The temperature quickly fell to normal and remained so. He was discharged on the 18th day of the disease, almost completely deaf in both ears.

Six months after discharge he was completely deaf in both ears.

*Discussion.*—In this case, apparently, a very severe infection, 1 injection rendered the spinal fluid sterile. The usual order of disappearance of symptoms and signs followed. The great diminution in

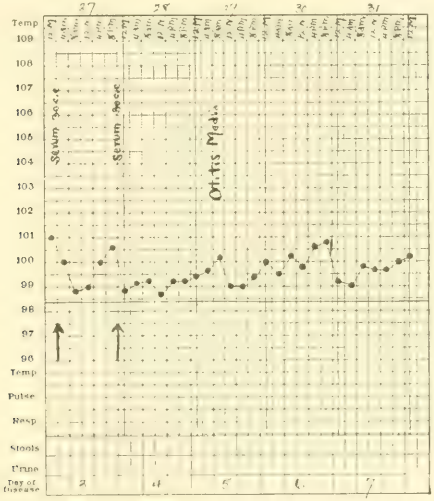



Chart No. XII. H. L. B. March, 1908.

the circulating leucocytes after 1 injection is strikng. The persistent elevation of temperature is probably coincident with the otitis media, and the previous attack is a large factor in the severity of the sequela. The desire to defecate produced during the first injection was constant, and would disappear if the injection was stopped.

From the symptoms and signs it is fair to say that this case recovered abruptly, and to attribute the subsequent fever to the otitis media. Relief of the latter was immediately followed by a normal temperature.

Case No XIII.—Hospital No. 63,238.

*Cerebrospinal meningitis (epidemic); acute; 3 injections of serum (30 cc. each); petechial eruption; double bronchopneumonia; improvement in spinal fluid; myocarditis; death; autopsy.*

N. S., a negress, æt. 25, was admitted upon the 3d day of her attack. The onset was with abdominal pain. Later she had a chill and became restless and feverish. The next day she moaned and moved her limbs constantly.

On admission she was in constant jerking motion, very restless, and crying without interruption. A macular eruption was noted over arms, chest, and back. She complained of headache and pain in the neck. There was no retraction of the head or arching of the back. The neck was stiff and motion painful. There was a divergent squint and a bilaterally positive Kernig sign.

A polymorphonuclear leucocytosis of 36,080 was present.

*Lumbar Puncture No. 1* was done on the 4th day.

Pressure—600+ mm.
Fluid removed—31 cc.
Antimeningitis serum injected—30 cc.

The fluid was very cloudy with large endothelial cells, small mononuclears, and a predominating number of polymorphonuclear leucocytes. Routine cultures yielded *Diplococcus intracellularis meningitidis;* 200 colonies to the tube. But in the sediment of the spinal fluid they were not definite—poorly staining groups, both intracellular and extracellular.

The temperature was not affected, remaining about on the level of 102° F.

She went into a deep stupor. Her respirations were 50 per minute, and her lungs showed a definite bronchopneumonia on both sides.

In 18 hours her neck was less stiff and her strabismus had cleared. She seemed more awake and complained of the infusion needle—which she had not noticed previously.

*Lumbar Puncture No. 2* was done on the 5th day, 20 hours after No. 1.

Pressure—495 mm.
Fluid removed—30 cc.
Antimeningitis serum injected—30 cc.

The injection caused her to squirm and groan, and from her motions one would judge there was pain in the legs.

The fluid was extremely cloudy and the polymorphonuclears were increased. The diplococci were more intracellular and less extracellular than before, and they stained indistinctly.

Routine cultures yielded 7 to 9 colonies per tube.

The leucocytes 5 hours later were 24,600. The temperature remained 102° F. to 103° F. The neck was still stiff and the Kernig sign positive. The respiratory distress was more marked and the lungs seemed to be filling up with crackles everywhere.

*Lumbar Puncture No. 3* was done on the 5th day, 12 hours after No. 2.

Pressure—210 mm.

Fluid removed—19 cc.

Antimeningitis serum injected—30 cc.

The fluid, still very cloudy, became bloody toward the end. No extracellular diplococci were seen and those in cells were very indistinct. Routine culture yielded 1 colony in 1 tube and none in the other.

Following this, the temperature was even higher, rising to 103.6° F. Her respirations were very shallow and with great effort. Herpes labialis appeared. She could not be roused.

The lungs showed no definite consolidation, but there was evidence of advanced bronchopneumonia in both lungs. Movements of the head seemed painful, the neck was stiff, and the Kernig sign bilaterally positive.

She suddenly became pulseless and died, the respirations apparently ceasing after the heart beat.

Several examinations of the urine, showed a heavy precipitate of albumen with hyaline and granular cells.

*Autopsy* (*No. 3036*) was performed by Dr. Krause, the notes of which follow:

*Anatomical Diagnosis.*—Acute purulohæmorrhagic leptomeningitis (brain and spinal cord). Acute purulent ethmoidal and sphenoidal sinusitis. Acute lobular pneumonia (bilateral). Acute mucopurulent bronchitis. Acute splenic tumor. Cloudy swelling of the viscera. Chronic cystitis. Multiple accessory spleens.

*Body* is that of a very stout mulatto woman, 175 cm. in length. Rigor mortis is present. There is no livor mortis. Over the front of the chest and abdomen are a number of small irregular areas, measuring from 2 mm. to about 1 cm., which are slightly darker in color than the rest of the skin but are not raised. The left pupil measures 6 mm., the right 4 mm. in diameter. There is no glandular enlargement and no œdema. The body fat is well preserved. The interior of the body is still warm. The coils of intestines in the pelvis are of a brownish-yellow color and feel as though the walls are infiltrated with bubbles of gas. The appendix region is normal. The spleen is in its normal position and is not adherent. The liver extends 5½ cm. below the ensiform cartilage. The diaphragm extends to the 5th rib on the left and 3d interspace on the right side. In the pelvis is a slight amount of blood-stained fluid. The left side of the thorax is clear as is also the right side. In the pericardial cavity there is a slight excess of clear straw colored fluid. The surfaces of the pericardium are clean.

*Heart* weighs 300 gm. There is a considerable excess of epicardial fat. The exterior of the heart is rather blue. The right side of the heart is normal although it is slightly bluer in appearance than normal. The valves are thoroughly competent. The mitral and aortic valves are normal. At the base of the aorta, just above the free edges of the flaps, there is a slight subintimal sclerosis. The coronary arteries are clear. The wall of

the left ventricle measures 16 mm. in width. The musculature is of normal consistence, and it is rather bluish-brown in color. It shows no patches of necrosis.

*Lungs.*—The right lung is about normal in size. It is crepitant throughout. In general it is rather pinkish-blue in color, although mottling the whole external surface are small grayish-pink patches. They will average from ½ to 1 cm. in diameter. The glands are normal at the hilum. In the bronchi is a small amount of mucopurulent material. The bronchial mucosa is rather œdematous and swollen. The cut section of the lung shows a very deep red surface, which is marked in both lobes by numerous rather granular and dry patches, which project above the rest of the surface. There are no apical scars in the lung. The left lung is about normal in size. It is rather heavier than normal. The pleura surface is smooth. Especially in the dependent parts, the lung is quite blue in appearance. Mottling the surface of this lung are the same grayish-pink patches that were noted in the right lung. When the lung is removed from the body considerable amount of pus exudes from the bronchus. This lung on section resembles the right in every respect, except the areas of consolidation are much more numerous, especially in the lower lobe.

*Spleen* weighs 200 gm., measures 17 x 8 x 6½ cm. Its capsule is smooth and a dark blue in appearance. It is normal in thickness. It was ruptured in removing the spleen from the body. The organ is slightly more flabby than normal. The cut surface is very dark reddish-brown in appearance, on which the markings cannot be made out before the pulp is scraped away. The pulp is very slightly increased in amount. The Malpighian bodies are normal in size. The frame-work of the spleen seems to be slightly more distinct than normal.

*Stomach* and *Duodenum* contain a small amount of orange colored mucoid material. There is quite a thick layer of mucus covering the whole interior of the stomach. The mucosa, however, is quite normal. Bile flows freely through the ampulla and there is no obstruction to be felt with the ducts.

*Pancreas.*—Between the pancreas and kidney there is a small accessory spleen, which is lobular in shape, measures about 2 cm. in diameter. The pancreas is normal in size and is a grayish-pink in color, and slightly softer than normal. Around the tail of the pancreas, in the mesentery, are seen 3 or 4 globular bodies, which vary in size from 4 mm. to 1½ mm. in diameter, which are made up of splenic tissue, and which present the same characteristic as the spleen itself. On section the pancreas is greatly congested and is rather softer than normal. The mesenteric glands are about normal.

*Liver* weighs 2150 gm., measures 32 x 21 x 9 cm. The external surface is smooth and uniform. The lobulations are easily made out on the external surface. The cut surface is rather opaque and cloudy. The lobulations are regular. There seems to be a slight increase in amount of fibrous tissue in the portal spaces. Here and there are small opaque yellowish dots, which suggest necrosis.

*Adrenals* seem slightly larger than normal. The cut surface shows a great excess of medulla, which is dark brownish-red in color. The cortex is represented by a very thin line. The whole cut surface is rather cloudy and opaque.

*Kidneys* weigh 440 gm. The *left* kidney measures 12 x 7 x 5 cm. Its capsule strips easily, leaving a smooth, cloudy, somewhat opaque grayish-pink surface. Longitudinal section through the kidney shows a very hazy cloudy surface which applies to both pyramids and cortex. The cortex is swollen but is regular in width, measures 9 mm. The striations are very much swollen. The Malpighian bodies stand out very prominently as bright red points in the surrounding grayish parenchyma. The pyramids are rather blue, although this blue appearance is broken up by cloudy grayish streaks, which traverse them. The *right* kidney measures 12 x 7 x 5 cm. and resembles the left in every respect.

*Retroperitoneal glands* are somewhat enlarged, rather moist and œdematous. The cut section is a pink-gray in color but fairly uniform.

*Intestines* are normal.

*Bladder. Rectum.*—Rectum is normal. The bladder contains a very small amount of purulent urine. The surface of the mucosa is somewhat roughened and is marked by numerous fine small hæmorrhages. The mucosa is also thicker than normal.

*Aorta* is normal and shows no sclerosis. The *œsophagus* is normal.

*Larynx* contains a great deal of mucopurulent fluid.

*Uterus* is normal in size. Its surface is smooth. The tubes are normal.

*Brain.—Dr. MacCallum's Note.*—On removal of the scull cap, the interior portion of the brain, on the right side, is found to be very much congested, even more than on the left side and there are hæmorrhages in the pia. On removal of the brain, it is found that the anterior portions of both temporal lobes, as well as the front of the right hemisphere, are very deeply congested and hæmorrhagic. The convolutions are a deep red in color and a diffuse hæmorrhage is accentuated by scattered spots of almost black color. Over the optic chiasm and base of the brain behind these and extending over the medulla and upwards over the cerebrum, especially over the left side, there is a thick greenish-white exudate, which covers everything in view. This exudate extends also over the top and back of the cerebrum, and at the extreme posterior part there are areas of hæmorrhage similar to those on the temporal lobes. Over the convexity of the cerebrum there is a great congestion, but the exudate is not very abundant, still it is to be observed especially on the right side and accompanying the great distended veins. The right cerebral ventricle is not greatly distended but contains a turbid fluid. The base of the ganglia is covered with a soft exudate, which can be easily scraped away. The left ventricle contains similar material. On section the hæmorrhages described in the temporal lobes are very superficial and appear as diffuse red and blackish dots along the edge of the surface, extending into each sulcus. The hypophysis is partly covered with exudate.

*Ear.*—The middle ear on both sides is clean. The ethmoidal and sphenoidal cells are filled with a purulent fluid.

*Cord.*—The fluid in the spinal canal is not greatly increased in amount. The external surface, of the dura, seems normal. The internal surface of the dura is smooth and slightly congested. The arachnoid membrane is quite thick, and binding it with the pia is a thick yellowish exudate of a fibrinopurulent character. There is considerable congestion of the cord but it is extremely soft.

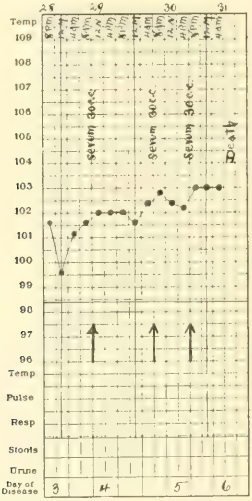



CHART No. XIII.—N. S. March, 1908.

*Discussion.*—This case, a very severe infection, showed in the spinal fluid the typical reactions of a healing process. The content of pus cells was increased at the expense of the circulating leucocytes. The organisms became intracellular and the cultures almost sterile. Certainly the number and the viability of the diplococci were very greatly affected by the serum.

The constantly elevated temperature was observed in both the other cases with complicating pneumonia.

Death was apparently due to myocarditis. She was a very large, fat woman, and it was expected that her heart muscle would not stand much strain.

If the pneumonia had been due to the meningococcus, subcutaneous injections of serum might have relieved the toxæmia.

Case No. XIV.—Hospital No. 63,291.

*Cerebrospinal meningitis (epidemic); acute; 7 injections of serum (30, 30, 30, and 15 cc. each); petechial eruption; bronchopneumonia; panophthalmitis; blindness; recovery.*

B. N., a white girl, æt. 9, was sent to the hospital by Dr. Rytina, on the 3d day of the attack. The onset was sudden, with headache and vomiting at night. The next day fever and delirium were present. A petechial eruption appeared over the body.

On admission, she was in a noisy, muttering delirium. The petechial eruption was apparent everywhere. The neck was stiff and head retracted. A periodic convergent squint was present. The conjunctiva of the right eye was injected and discharged pus. The lungs showed a slight bronchitis. The abdominal reflexes were absent. The Kernig sign was present on both sides.

There was a polymorphonuclear leucocytosis of 32,600.

*Lumbar Puncture No. 1* was done on admission on the 3d day.

Pressure—550 mm.
Fluid removed—23 cc.
Antimeningitis serum injected—30 cc.

The fluid was very cloudy with numerous polymorphonuclear leucocytes and a few endothelial cells. The *Diplococcus intracellularis meningitidis* was present, mainly extracellular in form. The great number of organisms, their large size and deep staining property, and the occurrence in chains of pairs rather than in groups of fours were striking features. Routine cultures yielded 76 colonies per tube.

The temperature remained practically unchanged, 101° F. to 102° F. There was no change in general condition. The right eye was even more injected and the cornea was clouded.

Leucocytes in 24 hours were 27,400.

*Lumbar Puncture No. 2* was done in 24 hours, on the 4th day.

Pressure—400 mm.
Fluid removed—30 cc.
Antimeningitis serum injected—30 cc.

The patient wriggled and cried out during the injection.

The fluid was even more cloudy than previously. While the polymorphonuclear leucocytes were increased, diplococci were hard to find and those seen stained poorly. Intracellular forms far outnumbered extracellular. Routine cultures yielded no growth.

In 12 hours the temperature had fallen to 100.6° F.; the leucocytes to 15,000. She was still delirious, her neck was stiff, and the Kernig sign was positive. The condition of the right eye was worse, showing pericorneal redness and pus in the anterior chamber. The spleen became palpable.

Then the temperature rose to a level of 102° to 103° F. The respirations were rapid. Herpes appeared on the lips, and the lungs showed

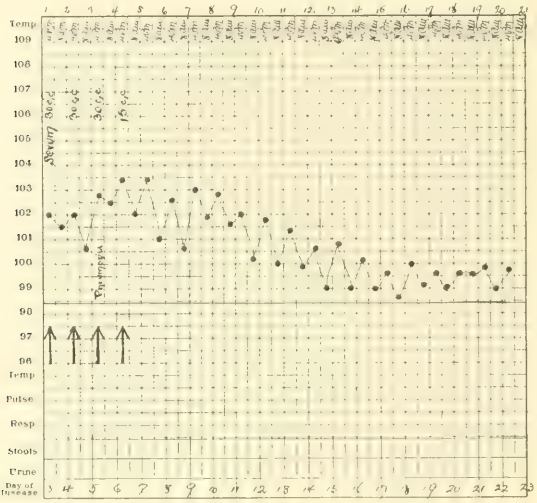



CHART No. XIV.—B. N. April, 1908.

scattered areas of bronchopneumonia. Although the last specimen of spinal fluid was sterile, still the elevated temperature and little if any change in signs caused

*Lumbar Puncture No. 3* to be done on the 5th day.

Pressure—500 mm.
Fluid removed—33 cc.
Antimeningitis serum injected—30 cc.

The fluid was not so cloudy as previously, polymorphonuclears being diminished in number and diplococci very few—all intracellular. Routine cultures showed no growth.

Following this injection, the signs of meningitis began to clear. She became rational; the eyes were straight and the rigidity less.

*Lumbar Puncture No. 4* was done on the 6th day.

Pressure—250 mm.

Fluid removed—21 cc.

Antimeningitis serum injected—15 cc.

She cried out constantly during the injection.

The fluid was markedly clearer, and only a few diplococci were indistinctly seen in polymorphonuclear leucocytes. Routine cultures were sterile.

In 24 hours the leucocytes were 13,600. The improvement was marked. Her mind was absolutely clear. Only a slight stiffness of the neck remained.

She very suddenly developed œdema of the face, puffy eyelids, and œdematous hands and forearms. The ankles and feet were free. Though the urine contained some albumen and white blood corpuscles, this condition was attributed to the large amount of serum she had received.

Coincident with the rise in temperature following the 3d puncture on the 5th day, the signs of bronchopneumonia became pronounced, especially in the right lower lobe. The signs of meningitis entirely disappeared. The temperature remained between 101° F. and 103° F. until the 11th day, when the bronchopneumonia was decidedly less marked. It then fell very gradually to normal, which it reached on the 30th day.

The condition of the right eye grew progressively worse. The iris became muddy, the humors purulent, the media clouded, the lids œdematous, and the retina detached. Panophthalmitis, a metastatic infection from the meninges, was diagnosed by Dr. Randolph. Sight was entirely lost.

Except for the loss of this eye, she was discharged in excellent condition on the 33d day.

*Discussion.*—This is another case of a severe infection with complications. The temperature did not fall after the administration of serum, but the spinal fluid remained sterile after 1 injection. The signs and symptoms of meningitis disappeared. Perhaps only one injection of serum would have been necessary. It seems likely that subcutaneous applications of the serum for its antitoxic property would have been valuable, inasmuch as the complications were probably metastatic infections.

The peculiar œdema was probably due to the foreign serum. Note the petechial eruption in this severe case with the complicatng pneumonia as in Case No. XIII.

Case No. XV.—Hospital No. 63,308.

*Cerebrospinal meningitis (epidemic); acute; 2 injections of serum (30 cc. each); recovery by lysis; no complications or sequelæ.*

F. N., white, male, æt. 11, was taken ill with headache and vomiting 2 days after his sister, B. N. (Case No. XIV), and sent into the hospital by Dr. Rytina the day after her admission. He had been delirious with a high fever, and had complained bitterly of being touched.

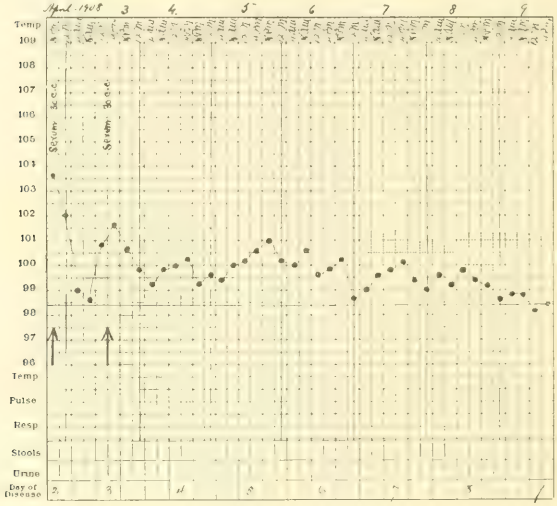



Chart No. XV.—F. N.

On the ward he was stupid and in a muttering delirium. His neck was quite stiff and movements were very painful. The Kernig sign was bilaterally positive. Over the abdomen were a few red macules, which did not disappear on pressure.

The polymorphonuclear leucocytosis amounted to 40,600.

*Lumbar Puncture No. 1* was done on the 3d day of the disease.

Pressure—500 mm.

Fluid removed—30 cc.

Antimeningitis serum injected—30 cc.

The injection caused movements of the legs suggesting pain and necessitating deep anæsthesia (general chloroform).

The fluid was very cloudy, showing a few small mononuclears, many large endothelial cells, and a predominating number of polymorphonuclear leucocytes. The *Diplococcus intracellularis meningitidis* was present in small numbers, equally intra- and extracellular. They stained distinctly. Routine cultures yielded 25 to 50 colonies per tube.

In 24 hours the temperature fell from 103.6° to 99° F., but soon rose again to 101.6° F. His general condition was unchanged. In his delirium he got out of bed and fell, bruising himself. A crop of herpes labialis appeared.

The leucocytes 17 hours after the injection were 31,200.

*Lumbar Puncture No. 2* was done on the 4th day, 18 hours after No. 1.

Pressure—600+ mm.

Fluid removed—45 cc.

Antimeningitis serum injected—30 cc.

The fluid was quite bloody and about as cloudy as the first specimen. However, the polymorphonuclear leucocytes seemed increased. The very few organisms seen were intracellular forms. Routine culture gave no growth.

Although the temperature fell by lysis and did not become regularly normal until the 16th day, still no more serum was injected on account of the marked improvement in the patient. His mind cleared up in 24 hours and his headache was relieved. In 48 hours, the Kernig sign and stiffness of the neck were disappearing. The leucocytes had fallen to 13,400.

His recovery was complete and he was discharged well on the 31st day.

*Discussion.*—This is another one of the pleasing cases in which the serum rendered the spinal fluid sterile after 1 injection. The symptoms and signs cleared with remarkable rapidity, although it required 12 days for the temperature to fall to normal.

It is interesting to note that this is the only case in the series in which direct contagion as the source of infection can perhaps be traced. It is possible, of course, that they both were infected from the same source instead of the girl infecting her brother.

Case No. XVI.—Hospital No. 63,425.

*Cerebrospinal meningitis (epidemic); acute; disappearance of organisms after 2 injections of serum (30 cc. each), and of symptoms after 3 injections (30 cc. each); toxic arthritis; intermittent fever, chills, and headache due to flare-up of spinal infection; abrupt recovery after 4th injection of serum (30 cc.); no sequelæ.*

P. J., male, negro, æt. 27, was admitted on the 6th day of the disease, which had developed during an attack of acute arthritis. The onset was marked by pain and stiffness in the neck, general discomfort, and vomiting. Later he had 2 convulsions, was unconscious, and had retraction of the head and squint. The pain in his head was very severe.

On examination he was stupid, complaining of pain in the arms and legs whenever touched. There was internal strabismus, rigidity of the neck, and a positive Kernig sign. Herpes labialis was present. The leucocytes were 12,000, mainly polymorphonuclears.

*Lumbar Puncture No. 1* was done on the 7th day of the disease.

Pressure—200 mm.

Fluid removed—18 cc.

Antimeningitis serum injected—15 cc.

The patient complained during injection of crampy pain in the right hip and leg—"wanted to stretch."

The fluid was quite cloudy and contained many flocculi. The leucocytes, 1383 to the cubic millimeter, were mainly polymorphonuclears. *Diplococcus intracellularis meningitidis* was present in enormous numbers, mainly extracellular. Routine cultures yielded a heavy diffuse growth on each tube.

The temperature rose slightly after the injection, but the general condition was unchanged. The squint, herpes, stiff neck, retracted head, arched back, and positive Kernig sign remained.

The leucocytes were increased to 23,200 in 20 hours.

*Lumbar Puncture No. 2* was done on the 8th day.

Pressure—200 mm.

Fluid removed—20 cc.

Antimeningitis serum injected—30 cc.

He complained of cramps in the legs during the injection.

The fluid was more cloudy with polymorphonuclear leucocytes. No extracellular diplococci were found and the intracellular forms were few in number and indistinctly outlined. The cell count numbered 412,000 to the cubic millimeter. Routine cultures gave 6 colonies per tube.

Twenty-four hours later the circulating leucocytes were 31,200. The temperature preserved a level of 100° F. to 101° F. Headache, hyperæsthesia, and positive Kernig were still present. Rigidity seemed less.

*Lumbar Puncture No. 3* was done on the 9th day.

Pressure—150 mm.

Fluid removed—12 cc.

Antimeningitis serum injected—30 cc.

Again the injection caused great pain in the limbs.

The fluid was less cloudy. No diplococci were found and routine cultures remained sterile.

The day following the temperature averaged between 100° F. and 101° F. the improvement was marked. The rigidity had entirely disappeared and the Kernig sign was not positive. It was at this time that a puffiness appeared over the dorsum of both wrists. There was considerable tenderness and limitation of motion on account of pain. Dr. Baer diagnosed the condition as a toxic arthritis.

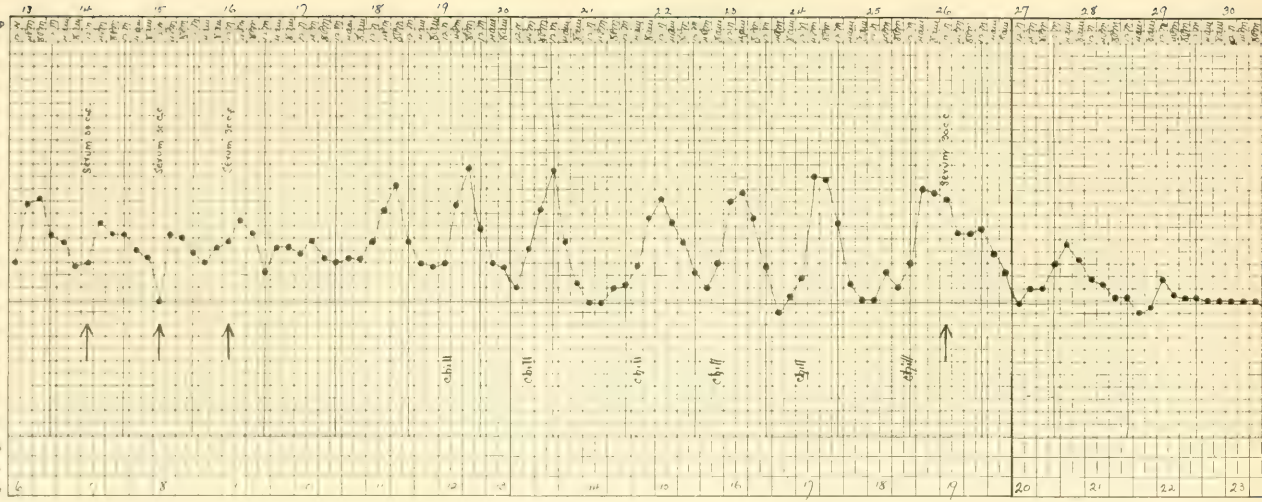



CHART No. XVI.—P. J. April, 1908.

Then followed a week of anxiety which would not occur a second time. During this period there occurred daily paroxysms of fever, initiated by chilly feelings, and occupying 22 hours on the average. The temperature would rise from normal to 103° F. and 104° F. usually in the afternoon. He would suffer severe occipital headache and be dull and stupid. Between paroxysms he was perfectly comfortable. The leucocytes were 22,000 and 18,400 during this time, 60 per cent of which were polymorphonuclears, and 22 per cent large mononuclears. No malarial parasites were found and no definite malarial pigment, although the large percentage of large mononuclear cells was noteworthy. The search for complications revealed nothing but the mild toxic arthritis. The blood culture was negative. An existing diarrhœa was relieved by discontinuing the salt solution per rectum.

Lumbar puncture was considered last because of the absence of the signs and symptoms of meningitis originally present, because the spinal fluid was sterile at the last tap, and because the intermittent character of the temperature suggested a complication rather than a flare-up.

*Lumbar Puncture No. 4* was done on the 19th day of the disease.

Pressure—510 mm.
Fluid removed—30 cc.
Antimeningitis serum injected—30 cc.

The fluid was very cloudy with polymorphonuclear leucocytes, and diplococci were present, mainly intracellular, in fair numbers. Routine culture yielded 1 to 2 colonies per tube.

The change following the injection of serum left no doubt as to the cause of the intermittent fever. In 22 hours the temperature reached normal and remained there almost steadily. His symptoms disappeared. The leucocytes were 6000 on the 27th day. He was discharged well upon the 51st day of the attack.

*Discussion.*—The intermittent fever seen in this case without any signs of meningitis, but undoubtedly due to a flare-up in the infection of the meninges, is a picture well worth remembering. One injection of serum was sufficient to turn the tide and end the trouble.

If the joint trouble had been more serious and due to a metastatic infection by meningococci, the local application of the serum would have been tried as in Dr. Ladd's case (J. Am. M. Ass., 1908, LI, 1319).

Case No. XVII.—Hospital Nos. 63,577 and 63,737.

*Cerebrospinal meningitis (epidemic); acute; 2 injections of serum (15 and 25 cc. each); acute lobar pneumonia; suppurative otitis media; lysis; empyema; operation; recovery.*

L. A., a white female, æt. 25 months, was sent into the hospital by Dr. Hardy on the 6th day of the disease. The day previous she had fallen and struck her head upon a couch. A severe nosebleed followed. The

onset was sudden with vomiting followed by stupor, fever, and headache. Stiffness of the neck and back developed 2 days before admission. She became hypersensitive, crying whenever touched.

On the ward she lay in a stupor. There was a divergent squint and the neck was stiff. The lungs were clear. Herpes labialis was present. The Kernig sign was negative.

The leucocytes were 40,400, mainly polymorphonuclears.

*Lumbar Puncture No. 1* was done on the 7th day of the disease.

Pressure—300 mm.
Fluid removed—24 cc.
Antimeningitis serum injected—15 cc.

The fluid was clear, except for fine flocculi. Microscopically no cells were seen—simply débris. *Diplococcus intracellularis meningitidis* was present in small numbers. Routine cultures yielded 1 colony per tube.

In 10 hours the leucocytes were 30,400. The temperature fell from 105° F. to 106° F. down to 101.4° F. The child was bright and apparently comfortable. The eyes were straight, but the neck still stiff.

*Lumbar Puncture No. 2* was done in 24 hours.

Pressure—160 mm.
Fluid removed—28 cc.
Antimeningitis serum injected—25 cc.

This caused the patient to squirm and cry out.

The fluid had become very cloudy with polymorphonuclears. A few indistinct diplococci were seen in cells. But routine culture yielded no growth.

Four hours before the puncture the temperature rose from 101.4° F. to 103° F., and this was not influenced by the injection. The signs of meningitis disappeared completely. The fever was accounted for by an area of consolidation in the upper portion of the left lower lobe.

The course following this was that of an acute lobar pneumonia involving the whole left lower lobe, terminating by lysis. On the 12th day a suppurative otitis media of the left ear was made evident by the spontaneous rupture of the tympanum and the discharge of pus. Cultures showed *Diplococcus intracellularis meningitidis* and *Staphylococcus pyogenes albus* present. On the 16th day the temperature had reached a level of 100° F. to 101° F. and the leucocytes were 24,600. On the 17th day the temperature rose again, reaching 104.9° F. on the 18th. And with this, signs of fluid in the left pleural cavity appeared. Exploratory puncture yielded a purulent pleural exudate. Whereupon she was transferred to the surgical side and the left pleural cavity drained.

In 10 days she was discharged from the surgical side as well. She was seen 4 weeks later in the outpatient department, where she was reporting for dressing. The wound was still discharging. She was in excellent condition and showed no other sequelæ.

*Discussion.*—The clear spinal fluid with flocculi in this case seems to indicate a healing process. The height of the temperature means less when one remembers her age—25 months. The signs of meningitis were moderately severe, and the spinal infection responded to 2 injections of serum.

The otitis media was a metastatic infection. But the pneumococcus seemed responsible for the pulmonary and pleural complications.

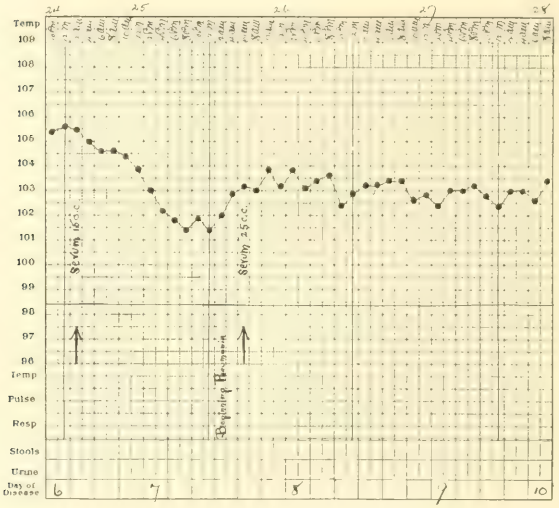



Chart No. XVII.—L. A. April, 1908.

Case No. XVIII.—Hospital No. 63,716.

*Cerebrospinal meningitis (epidemic); acute; mild case; abrupt recovery after 2 injections of serum (15 and 30 c.c. each); no complications or sequelæ.*

P. H., male, white, æt. 30, walked into the hospital on the 3d day of his attack, supported by friends. The onset was sudden with pains in the head, neck, chest, back, and legs, stabbing in character and periodic. His legs gave way and he had to be carried home from the street. Fever and vomiting were the other features.

On the ward he was generally hyperæsthetic and complained bitterly of paroxysmal attacks of pain. His neck was stiff and motion extremely painful. The Kernig sign was positive.

*Lumbar Puncture No. 1* was done on the 3d day of the disease.

Pressure—330 mm.
Fluid removed—24 cc.
Antimeningitis serum injected—15 cc.

The injection caused him intense pain in the knee-joints. He begged to be allowed to stretch his legs.

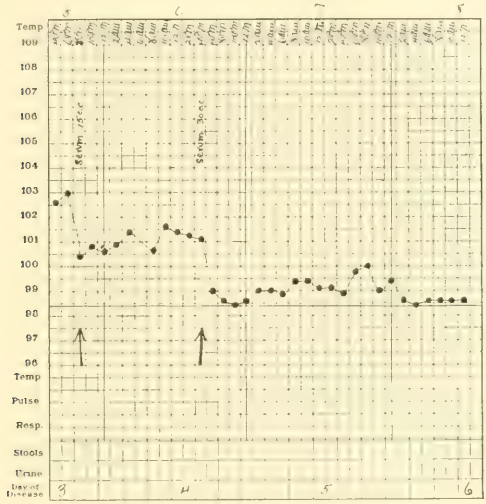



Chart No. XVIII.—P. H. May, 1908.

The fluid was quite cloudy, containing mainly polymorphonuclear leucocytes and a few small mononuclear and endothelial cells. *Diplococcus intracellularis meningitidis* was present, in and out of cells, few in number, but staining distinctly. Routine cultures gave 2 colonies per tube.

The leucocytes 15 hours later were 16,000. The improvement was marked. The temperature dropped from 103° F. to a level of 100° F. to 101° F. The headache was diminished, the neck fairly freely movable, and the Kernig sign no longer positive.

*Lumbar Puncture No. 2* was done 20 hours later on the 4th day.

Pressure—500 mm.
Fluid removed—65 cc.
Antimeningitis serum injected—30 cc.

The fluid was more cloudy than the previous specimen. The diplococci were in greater numbers, but all intracellular. Routine cultures remained sterile.

The temperature dropped to 98.5° F. in 4 hours and rose no higher than 100° F. thereafter. The leucocytes in 12 hours were 9200. Two days later he felt perfectly well, his temperature was normal, and the leucocytes were 6400. On the 7th day a profuse crop of herpes appeared on both lips. He was discharged well on the 13th day.

*Discussion.*—This, a very mild case, was cured rapidly by 2 injections of the serum.

Case No. XIX.—Hospital No. 63,817.

*Cerebrospinal meningitis (epidemic); acute; intermittent temperature; abrupt recovery after 3 injections (15, 30, and 30 cc. each); urticaria; no sequelæ.*

T. W. B., male, white, æt. 6, was admitted at the close of the 1st day of the attack. The onset was at night with sudden vomiting and involuntary passing of urine and fæces. Five hours previously he had fallen off the front steps and struck his head "a solid crack." Headache followed. Fever was noted after the vomiting and he became delirious. A few hours later he had a general clonic convulsion lasting five minutes.

On the ward, the neck was stiff and painful to motion. The Kernig sign was not present. The eyes showed a divergent squint. Otherwise the examination was not remarkable.

A polymorphonuclear leucocytosis of 35,600 was present.

*Lumbar Puncture No. 1* was done on the 2d day of the attack.

Pressure—180 mm.
Fluid removed—6 cc.
Antimeningitis serum injected—15 cc.

The fluid was bloody and only contained a few polymorphonuclears. No definite organisms were seen. But routine cultures gave a profuse growth of *Diplococcus intracellularis meningitidis.*

In 15 hours the leucocytes were 25,200. The temperature rose from 102.6° F. to between 104.4° F. and 106.4° F. He became even more stupid and seemed more severely intoxicated.

*Lumbar Puncture No. 2* was done 15 hours after No. 1.

Pressure—110 mm.
Fluid removed—18 cc.
Antimeningitis serum injected—30 cc.

The fluid was still bloody and the cell content seemed increased. Again no organisms were found. Routine cultures gave no growth.

The results were wonderful to observe. The temperature fell to 98.6° F. in 12 hours, and with it the signs and symptoms entirely disappeared. His mind was clear. His eyes were straight. No rigidity remained. The leucocytes were 13,200.

The temperature rose again, however, to 105.4° F. and

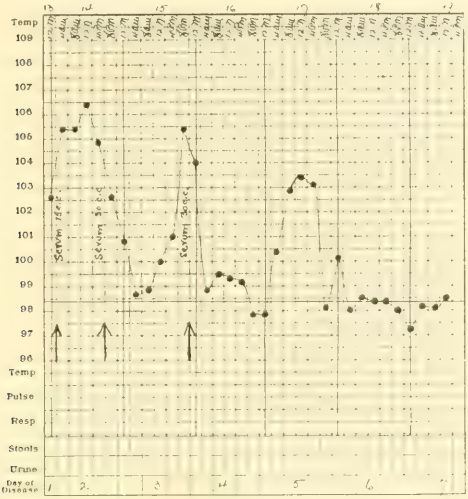



Chart No. XIX.—T. W. B. May, 1908.

*Lumbar Puncture No. 3* was done on the 3d day of the disease.

Pressure—110 mm.

Fluid removed—14 cc.

Antimeningitis serum injected—30 cc.

The fluid was more cloudy than previously, was only slightly blood tinged, and contained many polymorphonuclear leucocytes. Routine cultures remained sterile.

During the rise in temperature the patient became delirious and restless, but no rigidity or strabismus or signs of meningitis reappeared. Four hours after the serum injection the temperature was normal again. He

was bright and cheerful, without an ache or pain. The highest temperature on the 4th day was 100.4° F. On the 5th it rose to 103.4° F., but thereafter it remained about normal. On the 7th day he suffered from a profuse urticarial eruption.

He was discharged in excellent condition on the 11th day of the attack.

*Discussion.*—The remarkable intermittent temperature suggests Case No. XVI. The question arises: Did the serum cause the rapid drops in temperature? It does not seem probable. However, the astounding rapidity of disappearance of symptoms and signs after the second injection can certainly be considered due to it.

The first injection undoubtedly increased the toxæmia, most likely by its bactericidal effect. Evidence in favor of this is the bacteriological report of a "profuse growth" in No. I and "no growth" in No. II. Would not the subcutaneous application of a large dose of serum have prevented this by making use of its antitoxic property?

Case No. XX.*—Hospital No. 63,931.

*Cerebrospinal meningitis (epidemic); acute; 2 injections (30 and 15 cc. each); abrupt recovery; acrocyanosis two and a half months later as a sequela—erythromelalgia (?).*

G. G., male, white, æt. 15 yrs., was admitted to the clinic on the 2d day of the attack. The onset was with fever and drowsiness. Later he vomited. He walked into the hospital, but was quite irrational.

He was dull and stupid. The eyes rotated independently, producing a divergent squint. His neck was stiff and the Kernig sign was very suggestive, the test causing great pain.

There was a polymorphonuclear leucocytosis of 44,000.

*Lumbar Puncture No. 1* was done on the 2d day.

Pressure—260 mm.
Fluid removed—30 cc.
Antimeningitis serum injected—30 cc.

The fluid was only faintly cloudy and contained flocculi. Only a few cells, mainly polymorphonuclears were found, and some suspicious extracellular diplococci. Routine cultures gave a faint growth of *Diplococcus intracellularis meningitidis.*

The temperature was not influenced, but remained between 103° F. and 105° F. However, he became rational and said he felt better. His headache was gone. The stiff neck and bilateral Kernig sign persisted. The leucocytes in 24 hours were 26,400.

*Lumbar Puncture No. 2* was done 24 hours later, on the 3d day.

Pressure—75 mm.
Fluid removed—5 cc.
Antimeningitis serum injected—15 cc.

* Loc. cit. (14).

The fluid was quite cloudy, and the polymorphonuclears were increased. No definite organisms were recognized. Routine cultures yielded no growth.

Following this injection the temperature fell to normal in 24 hours and remained there. However it was 2 days before the rigid neck and the Kernig sign disappeared. The leucocytes on the 9th day were 10,800.

He was dischaged upon the 20th day in excellent condition.

He was admitted 2½ months later with a marked cyanosis of the hands and feet and the diagnosis of simple acrocyanosis made.

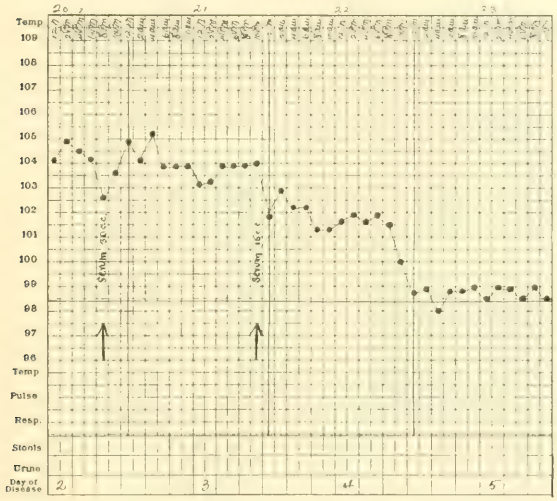



CHART No. XX.—G. G. May, 1908.

*Discussion.*—This case was quickly aborted by the serum, as is true of the 2 preceding cases. All 3 of them received the serum within the first 3 days of the attack.

This case, too, illustrates well the sequence of recovery. After the serum he suffered no symptoms, but was bright and cheerful—euphoric. The slight stiffness of the neck and positive Kernig sign persisted for 2 days after the 2d injection.

The acrocyanosis discovered two and a half months later has its

probable etiology in the attack of meningitis. It is particularly interesting in that now, six months later, the condition has progressed to almost an erythromelalgia. His feet and hands are a deep red color, and cause him considerable pain in cold weather, particularly when in the dependent position.

Case No. XXI.—Hospital No. 63,861.

*Cerebrospinal meningitis (epidemic); acute; 17 lumbar punctures and 12 injections of serum (5 of 15 cc., 6 of 30 cc., and 1 of 45 cc.); sterile spinal fluid after 3d injection; recrudescence at 9th puncture; paroxysms of fever and delirium; coma, slow pulse, and irregular respirations in crises; relief by lumbar puncture; respiratory paralysis; ventricular tapping; death after 18 hours of artificial respiration; autopsy.*

J. M., male, white, æt. 27 yrs., was admitted on the 8th day of his illness. The onset was with "freezings" followed by fever. The chills continued at various times during the week. He suffered severe headache and aching pains over the entire body. His neck and back felt stiff and sore. He had been confined to bed the last 4 days before admission.

On the ward he had a severe shaking chill. There was a profuse eruption of rose-red papules over his chest, abdomen, arms, and thighs, and some larger purpuric spots upon the lower legs. Attempts to move the head were vigorously resisted and caused great pain. The Kernig sign was bilaterally positive. There was a polymorphonuclear leucocytosis of 13,000.

*Lumbar Puncture No. 1* was done on the 9th day.

Pressure—160 mm.
Fluid removed—35 cc.
Antimeningitis serum injected—15 cc.

The fluid was quite cloudy with polymorphonuclears and a few small mononuclear and endothelial cells. A few intra- and extracellular diplococci were seen. Routine cultures yielded 2 colonies per tube of the *Diplococcus intracellularis meningitidis.*

The temperature continued to fall from 103.4° F. to 99.8° F. and rose again the next day. The leucocytes were increased to 22,500 in 24 hours. The general condition remained the same.

*Lumbar Puncture No. 2* was done on the 10th day, 20 hours after No. 1.

Pressure—400+ mm.
Fluid removed—65 cc.
Antimeningitis serum injected—30 cc.

The fluid was more purulent than previously, showing a great increase in polymorphonuclear leucocytes. Numerous diplococci were found in and out of cells, in apparently good health. Routine cultures gave a very heavy growth on each tube.

A drop in temperature to 100.2° F. followed, and the patient enjoyed a deep sleep. The headache, pain in the neck, and general hyperæsthesia persisted, however. In 36 hours he was resting comfortably, his temperature being 99.2° F. His pains were less, but the neck was still stiff and the Kernig positive. The leucocytes were 17,200.

*Lumbar Puncture No. 3* was done on the 12th day.

Pressure—420 mm.
Fluid removed—50 cc.
Antimeningitis serum injected—30 cc.

The fluid was less cloudy. Fewer cells were phagocyting, but those doing so contained more diplococci, 3 to 8 pairs in a cell. The organisms stained poorly. Routine cultures yielded 30 colonies per tube.

The temperature maintained a level between 99.5° F. and 101.8° F. The patient was greatly upset by the injection and cried with pain in the head for 4 hours afterward. The leucocytes reached 14,800 the next day.

*Lumbar Puncture No. 4* was done on the 13th day.

Pressure—250 mm.
Fluid removed—35 cc.
Antimeningitis serum injected—30 cc.

The fluid was much less cloudy and contained fewer polymorphonuclear and relatively more small mononuclear cells. Diplococci were only in cells, few in number and indistinct. Routine cultures gave no growth.

As previously, he tossed and screamed with pain for 3 hours after the injection. He complained particularly of a splitting headache. His neck remained stiff and the Kernig positive.

On the 15th day the temperature rose from the previous level of 101° F. to 103.8° F. The leucocytes were 11,200. He showed no intensification of signs and symptoms nevertheless.

*Lumbar Puncture No. 5* was done on the 16th day.

Pressure—320 mm.
Fluid removed—50 cc.
Antimeningitis serum injected—30 cc.

The fluid was distinctly less cloudy, and no definite organisms were seen. A few indistinct, intracellular forms were made out. Routine cultures gave no growth.

Three days later the leucocytes were 6440. His temperature varied from 100.8° F. to 103° F. He rested better, but the tenderness over the spine, the stiff neck, and the positive Kernig sign persisted.

*Lumbar Puncture No. 6* was done on the 19th day.

Pressure—410 mm.
Fluid removed—50 cc.
Antimeningitis serum injected—45 cc.

The fluid was even clearer than before. Microscopically the mononuclear elements were found increasing. No organisms were found in the sediment or in cultures.

The temperature fell to 98.2° F., only to rise again to 101° F. He was miserable, groaning with pain in his head, neck, back, in fact "all over." His head was retracted, neck stiff, and Kernig positive. A slight strabismus was present. All the signs and symptoms seemed intensified. The cause of this was considered to be probably the unusually large amount of serum injected—45 cc. Consequently to relieve this

*Lumbar Puncture No. 7* was done on the 20th day.

Pressure—450 mm.
Fluid removed—50 cc.
Antimeningitis serum injected—15 cc.

The fluid was quite clear, showing a few polymorphonuclear leucocytes and no organisms. Routine cultures gave no growth. The leucocytes before this injection were 11,200.

From now on he remained in practically the same condition. He was dull, stupid, and hard to rouse. He had a wild stare in his eyes. He would answer questions at times, and respond slowly to directions. He seemed to be deaf. The rigidity disappeared from the neck, although the Kernig remained positive.

His temperature would rise in paroxysms every 2 or 3 days with no regular periodicity, reaching 102° F. and 103° F., and falling in 12 to 24 hours. These were occasionally preceded by rigors and accompanied by sweating. During them he would be irrational and attempt to get out of bed. Between them the temperature varied from 98° F. to 100° F. The leucocytes were:

16,280 on the 27th day.
12,720 on the 28th day.
15,000 on the 31st day.
8,400 on the 37th day.

On the 27th day, during one of the febrile paroxysms,

*Lumbar Puncture No. 8* was done.

Pressure—360 mm.
Fluid removed—45 cc.
Antimeningitis serum injected—none.

The fluid was clear and contained a few polymorphonuclear leucocytes, but no organisms microscopically or in culture.

Search for a secondary infection, some pyogenic complication, was in vain. The ears, joints, chest, and abdomen showed nothing remarkable. Internal hydrocephalus was considered. Dr. Bordley noted on the 31st day that there were no signs of choked discs. And on this report Dr. Cushing considered hydrocephalus improbable and saw no indication for surgical interference.

During the febrile paroxysms on the 35th and 38th days he was nauseated and vomited. He was growing much weaker. His pulse was becoming rapid and poor in quality. His expression was very unnatural. He had a blank stare and would lie with his eyes open most of the time.

apparently seeing imaginary objects. Nystagmus and a coarse tremor of the hands developed.

On the 40th day

*Lumbar Puncture No. 9* was done.

Pressure—650+ mm.
Fluid removed—40 cc.
Antimeningitis serum injected—15 cc.

The fluid spurted over the end of the tube. It was faintly cloudy again and contained flocculi. Some suggestive extracellular diplococci were seen, but routine cultures gave no growth. Cultures made from the fluid after it was incubated 24 hours gave a faint but definite growth of meningococci.

On account of the return of organisms, it was thought advisable to push the serum treatment, and so

*Lumbar Puncture No. 10* was done on the 41st day.

Pressure—200 mm.
Fluid removed—20 cc.
Antimeningitis serum injected—15 cc.

The fluid was more cloudy even and the content of polymorphonuclear leucocytes was increased. No organisms were seen and routine cultures were negative.

*Lumbar Puncture No. 11* followed on the 42d day.

Pressure—400 mm.
Fluid removed—35 cc.
Antimeningitis serum injected—30 cc.

The fluid was clearing again, though many polymorphonuclears were present. No organisms were found microscopically or by culture

During these days his condition did not change in the slightest. On the 43d day he went suddenly into a state of collapse. He was conscious; his pulse was slow, 80 to the minute, and weak; and his respirations were labored. His pupils were small and would not react. The condition was attributed to a sudden increase in intracranial pressure, and so

*Lumbar Puncture No. 12* was done at once.

Fluid was under enormous pressure, spurting up out of a capillary tube, 600 mm. in length.

Fluid removed—40 cc.
No serum was injected.

The fluid was clouded with polymorphonuclears, but no organisms were seen or recovered.

The relief was instantaneous. His breathing became at once deep, free, easy, and regular. His pulse improved in quality, and he soon regained consciousness. His temperature rose from 98.4° F. to 103.7° F. 4 hours after the puncture.

Twelve hours later he was quite irrational and

*Lumbar Puncture No. 13* was done on the 43d day.

Pressure—200 mm.

Fluid removed—6 cc.

Antimeningitis serum injected—none.

The fluid was similar in character to that of No. 12.

At this time his emaciation was extreme. There was great danger of decubitus ulcers; he lost control of the bladder and anal sphincters; there was a facial asymmetry, the left side being fuller, more mask-like and showing a slight ptosis. No paralyses were evident. His neck was stiff and painful and the Kernig was positive. Otherwise the examination was negative. All the reflexes were present. The optic discs were not swollen. Heart, lungs, and abdomen remained clear. The temperature was still irregular, between 97.5° F. and 100° F. with occasional paroxysms to 103° F. and 104° F.

On the 46th day a fresh crop of herpes appeared in the district of the maxillary branch of N. trigeminus.

*Lumbar Puncture No. 14* was performed on the 46th day.

Pressure—250 mm.

Fluid removed—25 cc.

Antimeningitis serum injected—15 cc.

The fluid seemed to contain more small mononuclear leucocytes than previously, polymorphonuclears predominating however. Cultures remained sterile.

On the 48th day his respirations again became irregular and suddenly his pulse dropped from 120 to 60 to the minute. He lapsed into unconsciousness and soon ceased breathing. Artificial respiration was kept up while a *lumbar puncture* was hurriedly done (No. 15) to relieve the apparent sudden increase in intracranial pressure.

Pressure—was very great, the fluid spurting from the needle.

Fluid removed—50 cc.

Antimeningitis serum injected—none.

The fluid seemed to be more cloudy and the polymorphonuclear leucocytes increased. No organisms were recovered.

In 10 minutes after the tapping, 40 minutes after he had ceased breathing, he resumed it without artificial stimulus—at first weakly, but quite normally in 6 hours. Eight hours later he was conscious and in fairly good condition.

*Lumbar Puncture Nos. 16 and 17* were done on the 49th and 51st days. The pressure was still increased and the fluid sterile. No serum was injected.

On the morning of the 52d day, he stopped breathing for the 3d time. Artificial respiration was kept up. Lumbar puncture did not relieve him. It seemed to be impossible to draw off much spinal fluid. Six hours later

Dr. Cushing performed a *ventricular tapping* (No. 1). One hundred cubic centimeters of yellow, turbid fluid were withdrawn. This showed many polymorphonuclear leucocytes, but no organisms. Cultures gave no growth.

His pulse became gradually weaker. At one time he made 2 definite inspiratory efforts, but died finally 18 hours after he had ceased breathing.

*Autopsy* (*No. 3069*) was performed by Dr. Krause.

*Anatomical Diagnosis.*—Acute fibrinopurulent spinal leptomeningitis; chronic cerebral leptomeningitis (basal); chronic ependymitis; internal hydrocephalus; acute congestion of viscera (lungs, liver, kidneys, intestines, brain); chronic cystitis, ureteritis, and pyelitis; chronic splenic tremor; chronic adhesive pleuritis.

The notes on the brain and cord only interest us.

*Brain.*—There is considerable congestion of the vessels of the dura when this membrane is viewed externally. The dura is not abnormally adherent to the skull cap. The cerebrum seems slightly larger than usual, but the hemispheres are symmetrical. There is considerable injection of all the vessels of the brain. The dura is not adherent over the cerebrum, but on removing the brain, there were adhesions which bound the base and tips of the temporal lobes to the dura. No exudate is anywhere visible on the surface of the brain. The pia arachnoid is thickened over the whole base, thickest over the cerebellum, where it takes on a greenish semitranslucent appearance.

The brain was opened after hardening in formalin and the lateral ventricles were enormously distended. A thick greenish exudate lines the ependyma in places. The 3d and 4th ventricles as well as the central canal were also distended.

*Cord.*—The internal surface of the dura is smooth. Between the arachnoid and the cord and completely surrounding the cord, there is a thick, creamy, opaque, yellowish, greenish exudate. This exudate, however, is more abundant over the dorsal surface of the cord. It extends throughout the whole length of the cord. The cord itself does not seem to be involved. The blood-vessels are everywhere enormously congested. There is no fluid noted between the dura and the arachnoid.

*Discussion.*—This case received serum first on the eighth day of the disease. It did not impress one as a very severe attack, but the presence of a petechial eruption and the fact that it required 3 injections of serum to render the spinal fluid sterile are evidences of a flourishing infection.

The stupid, dull mental state, the wild stare in the eyes, the intense headaches, the crises with slowed pulse and embarrassed respiration, suggest associated hydrocephalus. Add to these the fact that when a ventricular tapping was finally done, just before death, a large amount (100 cc.) of fluid was withdrawn—which was under considerable pressure. Against it is the absence of changes in the optic discs.

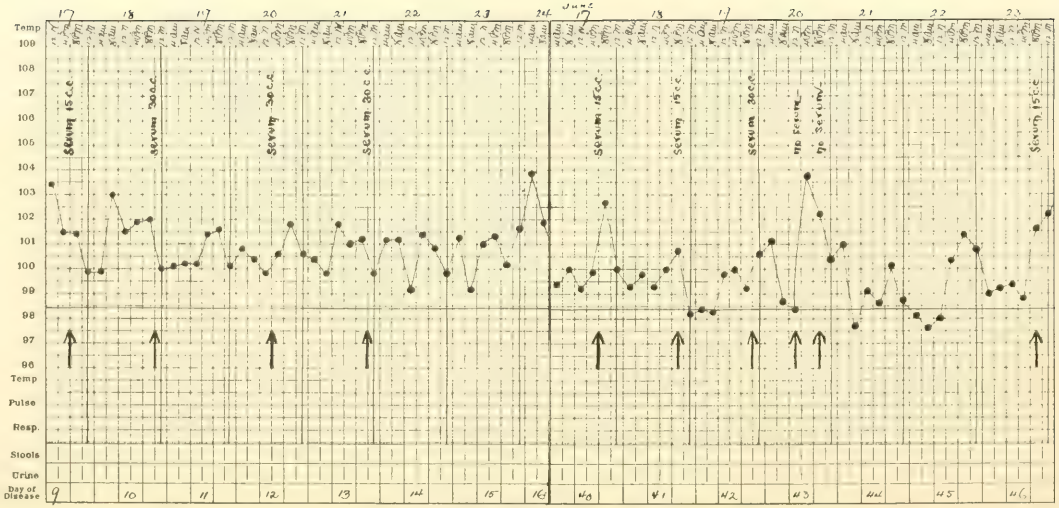



Chart No. XXI.—J. M. May, 1908.

That the lateral ventricles did form a habitat for the meningococci, out of reach of the serum introduced intraspinally, seems sure. The paroxysms of fever, in the absence of a focus elsewhere that could be demonstrated clinically or by the pathologists, the subsequent recrudescence of the spinal infection discovered at the ninth puncture on the fortieth day, the turbidity of the ventricular fluid removed by ventricular puncture on the fifty-second day, in spite of the fact that no organisms were demonstrable at this date, and the autopsy findings—all are evidences of a pyohydrops ventriculorum which the cause of this unfortunate man's death.

Undoubtedly ventricular puncture and introduction of serum should have been performed early in the disease when the paroxysms of fever and the apathy were developing although a clear and sterile spinal fluid had been found.

The three crises in which respiration ceased, the pulse was slowed, and coma produced are interesting. They were due to a sudden increase in the intracranial pressure. The relief obtained from lumbar puncture in the first two would seem to point to an open communication between the spinal arachnoid space and either the cerebral subarachnoid space or the lateral ventricles. In the final crisis, however, which caused his death, a very little fluid could be drawn off by the lumbar route, when the ventricular tapping showed the lateral cavities of the brain distended with fluid under pressure.

Case No. XXII.—Hospital No. 64,242.

*Cerebrospinal meningitis (epidemic); acute; 1 injection of serum (20 cc.); abrupt recovery; no sequelæ.*

H. D., negro, æt. 27 yrs., was taken sick 4 days before admission with drowsiness and general malaise. He fell upon the street on account of weakness in the knees. He had severe headache and pain in the neck, back, and hips. Chills occurred daily for 3 days and fever had been constant.

On the ward he was delirious. His neck was stiff and his head retracted. The Kernig sign was bilaterally positive. Otherwise the examination revealed nothing remarkable.

There was a polymorphonuclear leucocytosis amounting to 16,300.

*Lumbar Puncture No. 1* was done on the 6th day of the disease.

Pressure—380 mm.
Fluid removed—2 cc.
Antimeningitis serum injected—20 cc.

The puncture was done at a clinic for demonstration. Local anæsthesia was used. The resistance of the patient resulted in breaking off the needle,

necessitating a small incision to remove the point. Through this incision the 2d needle was introduced. But the fluid was very purulent and ran so slowly that only 2 cc. were obtained.

The fluid contained polymorphonuclear leucocytes in great abundance and the *Diplococcus intracellularis meningitidis* in and out of cells. The diplococci were mainly extracellular and they stained clearly and deeply. Routine cultures yielded 18 colonies per tube. The temperature was 103.8° F. 4 hours later and then fell to 98.5° F. in 12 hours. With the

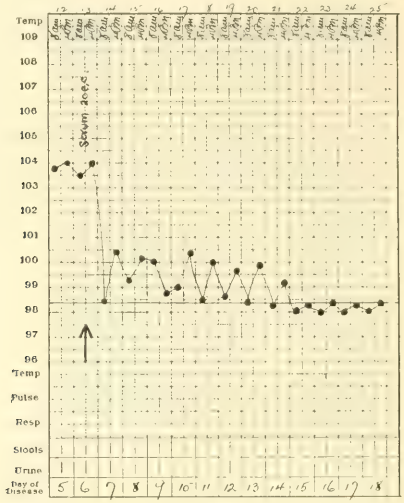



Chart No. XXII.—H. D. June, 1908.

rapid fall, he became rational, complained only of pain in the incision and slept most of the time. His neck was only slightly resistant and painless. The Kernig sign disappeared.

The leucocytes 48 hours after the injection were 16,200.

The temperature did not remain normal until the 15th day, but showed afternoon rises, diminishing in height each day. Convalescence was uneventful and he was discharged on the 19th day in excellent condition.

*Discussion.*—This is the only case in the series in which the fluid was so purulent and flowed so slowly that only a few centimeters were removed. Notwithstanding this fact, it was thought best to inject a

large amount of serum—20 cc. The rapid crisis resulting justified the move.

The broken needle in this case is the only instance of such a complication in the experience of the clinic in the last 4 years. As a routine now, the flexible irido-platinum needles are employed—needles which can be bent double without breaking.

Case No. XXIII.—Hospital No. 64,299.

*Cerebrospinal meningitis (epidemic); acute; chronic nephritis; convulsions; 1 injection of serum (10 cc.); lysis; no sequelæ.*

F. G., a negress, æt. 17 yrs., was brought to the hospital in coma. Her friends could not give a clear history and she herself on recovery remembered nothing about the onset. She had probably been ill for 5 days with fever, delirium, and occasional convulsions.

On the ward she immediately had a general convulsion lasting 1 minute, during which she stopped breathing and artificial respiration was resorted to. She was unconscious after this. Her eyelids were puffy and œdematous. There was a divergent squint. Her tongue was swollen where she had bitten it during a convulsion. The Kernig sign was negative. There was no stiffness of the neck or back; no hypersensitiveness.

There was a polymorphonuclear leucocytosis of 25,000.

The urine had a specific gravity of 1016, and contained albumen, 2 g. to the litre, and hyaline, waxy and granular casts and a few red blood corpuscles.

*Lumbar Puncture No. 1* was done on the 6th day of the disease.

Pressure—400 mm.
Fluid removed—11 cc.
Antimeningitis serum injected—none.

The fluid was clear with a few flocculi. Polymorphonuclear leucocytes predominated, but the cell content was small and no organisms were seen. Routine cultures gave no growth. The temperature, 98.5° F. at the time of puncture, rose to 101° F. after it. She was more rational, but no marked improvement occurred. The physical signs were unchanged.

On the following day she had 2 convulsions, and

*Lumbar Puncture No. 2* was done on the 8th day.

Pressure—250 mm.
Fluid removed—20 cc.
Antimeningitis serum injected—10 cc.

The fluid was slightly clouded, showing a few polymorphonuclear leucocytes and degenerated mononuclears. No organisms were seen, but routine cultures yielded the *Diplococcus intracellularis meningitidis*, 3 colonies per tube.

The temperature rose in 2 hours from 99.2° F. to 102.6° F. and fell by lysis, reaching and remaining normal from the 23d day. The leucocytes fell to 14,000 in 48 hours. Her mind cleared rapidly and symptoms disappeared. She convalesced rapidly and was discharged on the 28th day.

She passed large amounts of urine throughout, of a low specific gravity, and constantly containing albumen and casts. This was present on discharge.

*Discussion.*—The question of uræmia complicated this case on admission. The convulsions, œdema, character of urine, absent rigidity and Kernig sign, and clear spinal fluid led to omitting the injection of serum at the first puncture. This was a mistake. The patient

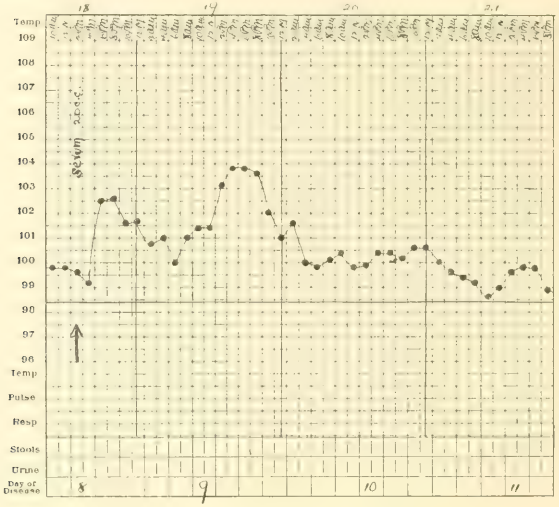



Chart No. XXIII.—F. G. June, 1908.

should receive the benefit of the doubt. But this mistake led to a positive diagnosis.

As was not infrequent before the use of serum, the first lumbar puncture and removal of fluid alone led to an apparent flare-up, the clouding of the fluid and the presence of organisms. Contrast this with the marked improvement after the injection of only 10 cc. of serum.

The chronic nephritis was incidental and not accredited to the meningitis.

Bibliography.

1. Barker, L. F.: Johns Hopkins Hosp. Bull., 1908, XIX, 94.
   Sladen, F. J.: Johns Hopkins Hosp. Bull., 1908, XIX, 245.
   ——— J. Am. M. Ass., 1908, LI, 1318.
   ——— Old Dominion J. Med. and Surg., 1908, VII, 241.
   ——— Trans. Oregon State Med. Assoc., 34th Annual Meeting, 1908, 198.
2. Flexner, Simon, and Jobling, J. W.: J. Exper. Med., 1908, X, 141.
   ——— Idem, 1908, X, 690.
   ——— J. Am. M. Ass., 1908, LI, 269.
   ——— Trans. Ass. Amer. Physicians, 1908, XXIII, 76.
   ——— Idem, 24th Annual Meeting, 1909.
   ——— Zentralbl. f. inn. Med., 1908, XXIX, 893.
   ——— Arch. Pediatrics, 1908, XXV, 747.
3. Koplik, Henry: Med. Record, 1908, LXXIV, 557.
4. Dunn, C. H.: Boston Med. and Surg. J., 1908, CLVIII, 370.
   ——— Idem, 1908, CLIX, 743.
   ——— J. Am. M. Ass., 1908, LI, 15.
   ——— Arch. Pediatrics, 1908, XXV, 756.
   ——— International Clinics, 1908, IV, 251.
5. Robb, A. G.: Brit. Med. J., 1908, I, 382.
   ——— Idem, 1908, II, 1341.
6. Ker, C. B.: Edinburgh Med. J., 1908, I, 306.
   ——— Brit. Med. J., 1908, II, 1340.
7. Ladd, L. W.: J. Am. M. Ass., 1908, LI, 1315.
8. Fulton, F. T.: Boston Med. and Surg. J., 1908, CLIX, 537; 572; 617.
9. Chase, W. S., and Hunt, M. L.: Arch. Int. Med., 1908, I, 294.
10. Morgan, J. D., and Wilkinson, W. W.: Arch. Int. Med., 1908, II, 253.
11. Churchill, F. S.: J. Am. M. Ass., 1908, LI, 21.
    ——— Idem, 1909, LIII, 841.
    ——— Arch. Pediatrics, 1908, XXV, 754.
12. Miller, A., and Barber, S. A.: J. Am. M. Ass., 1908, I, 1975.
13. Cushing, H., and Sladen, F. J.: J. Exper. Med., 1908, X, 548.
14. Sladen, F. J.: Johns Hopkins Hosp. Bull., 1909, XX, 22.
15. Jobling, J. W.: J. Exper. Med., 1909, XI, 614.

16. Flexner, Simon, and Barker, L. F.: Amer. J. Med. Sci., 1894, CVII, 155; 259.
17. Flexner, Simon: J. Exper. Med., 1907, IX, 105.
18. ——— Idem, 1907, IX, 142.
19. ——— Idem, 1907, IX, 168.
20. Kolle u. Wassermann: Deutsche med. Wchnschr., 1906, XXXII, 609.
21. Wassermann: Idem, 1907, XXXIII, 1585.
22. Jochmann: Deutsche med. Wchnschr., 1906, XXXII, 788.
23. Schöne: Die Therapie der Gegenwart., 1907, XLVIII, 52.
24. Sachs, L. B.: Arch. of Diagnosis, 1909, II, 296.
25. Knox, J. H. M., and Sladen, F. J.: Arch. Pediatrics, 1908, XXV, 761.
26. Moeller, H. N.: Med. Record, 1908, LXXIV, 19.
27. Miller, R. T.: Amer. J. Med. Sci., 1908, CXXXVI, 781.
28. Weichselbaum: Quoted by Elser and Huntoon. J. Med. Research, 1909, XV, 371.
29. Jaeger: Ibid., J. Med. Research, 1909, XV, 371.
30. Elser and Huntoon: J. Med. Research, 1909, XV, 371.
31. Councilman, Mallory and Wright: Report of the State Board of Health of Massachusetts, Boston, 1898.
32. Osler, W.: Brit. Med. J., 1899, I, 1517.

# INDEX


Acute endocarditis with lobar pneumonia, 139.
Acute lobar pneumonia, Acute pericarditis complicating, 155.
Acute lobar pneumonia, Empyema in, 167.
Acute lobar pneumonia in the Johns Hopkins Hospital, from May 15, 1889, to May 15, 1905, An analytical study of, 55.
Acute lobar pneumonia, The leucocytes in, 89.
Acute pericarditis complicating acute lobar pneumonia, 155.
Analytical study of acute lobar pneumonia in the Johns Hopkins Hospital, from May 15, 1889, to May 15, 1905, 55.
Analytical study of terminal pneumonia, 99.
Arthritis, Pneumococcic, 229.
Bacteriological and clinical study of a series of seventy-four cases of diarrhœa in children, 1
Chatard, J. A., Acute pericarditis complicating acute lobar pneumonia, 155.
Chatard, J. A., An analytical study of acute lobar pneumonia in the Johns Hopkins Hospital from May 15, 1889, to May 15, 1905, 55.
Chatard, J. A., An analytical study of terminal pneumonia, 99.
Chatard, J. A., The leucocytes in acute lobar pneumonia, 89.
Davis, John Staige, Skin transplantation. With a review of 550 cases at the Johns Hopkins Hospital, 307.
Delayed resolution in lobar pneumonia, 277.
Diarrhœa in children, A bacteriological and clinical study of a series of seventy-four cases of, 1.
Emerson, Charles P., The termination of pneumonia in cases with recovery, 103.
Empyema in acute lobar pneumonia, 167.
Endocarditis, Acute, with lobar pneumonia, 139.
Epidemic cerebrospinal meningitis and serum therapy at the Johns Hopkins Hospital, 397.
Fabyan, Marshal, A pathological analysis of 195 cases of lobar pneumonia, 81.
Hanes, Frederic M., Pneumococcus meningitis, 247.
Howard, Campbell P., Pneumococcic arthritis, 229.
Knox, J. H. Mason, Jr., and Schorer, Edwin H., A bacteriological and clinical study of a series of seventy-four cases of diarrhœa in children, 1.
Leucocytes in acute lobar pneumonia, 89.
Lobar pneumonia, Acute endocarditis with, 139.
Lobar pneumonia, Delayed resolution in, 277.
Lobar pneumonia, A pathological analysis of 195 cases of, 81.

McCrae, Thomas, Delayed resolution in lobar pneumonia, 277.
McCrae, Thomas, Empyema in acute lobar pneumonia, 167.
Marshall, Harry T., Acute endocarditis with lobar pneumonia, 139.
Meningitis, Epidemic cerebrospinal, and serum therapy at the Johns Hopkins Hospital, 397.
Meningitis, Pneumococcus, 247.
Pathological analysis of 195 cases of lobar pneumonia, 81.
Pericarditis, Acute, complicating acute lobar pneumonia, 155.
Peripheral venous thrombosis in pneumonia with report of three cases and a review of those previously recorded, 189.
Pneumococcic arthritis, 229.
Pneumococcus meningitis, 247.
Pneumonia, Peripheral venous thrombosis in, with report of three cases, etc., 189.
Pneumonia, The termination of, in cases with recovery, 103.
Schorer, Edwin H., and Knox, J. H. Mason, Jr., A bacteriological and clinical study of a series of seventy-four cases of diarrhœa in children, 1.
Serum therapy, Epidemic cerebrospinal meningitis and, at the Johns Hopkins Hospital, 397.
Skin transplantation. With a review of 550 cases at the Johns Hopkins Hospital, 307.
Sladen, Frank J., Epidemic cerebrospinal meningitis and serum therapy at the Johns Hopkins Hospital, 397.
Steiner, Walter R., Peripheral venous thrombosis in pneumonia with report of three cases and a review of those previously recorded, 189.
Terminal pneumonia, An analytical study of, 99.
Termination of pneumonia in cases with recovery, 103.

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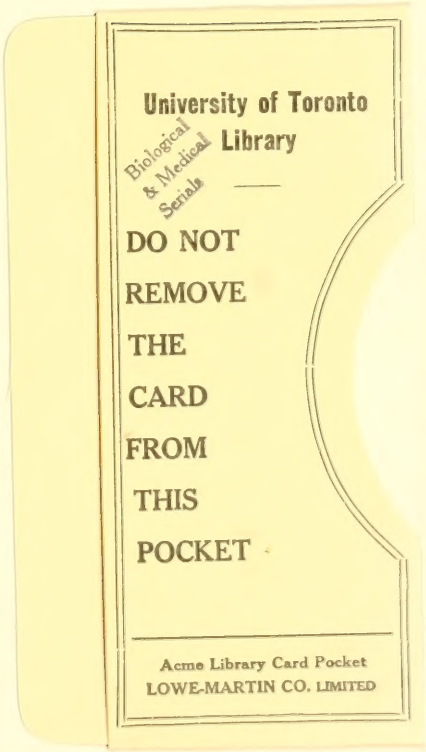
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